Opko Health, Inc.
Form 424B2
February 06, 2019
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Filed Pursuant to Rule 424(b)(2)

Registration No. 333-229400

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount of Securities to be Registered[1]	Proposed Maximum Offering Price	Proposed Maximum Aggregate Offering Price[1]	Amount of Registration Fee[2]
4.50% Convertible Senior Notes due 2025	$230,000,000	100% of principal amount	$230,000,000	$27,876
Common Stock, par value $0.01 per share	(3)	(3)	(3)	(3)

(1) Includes principal amount of notes which may be purchased by the underwriter to cover over-allotments, if any.
(2) Calculated pursuant to Rule 457(r) of the Securities Act of 1933, as amended (the Securities Act).
(3) Includes an indeterminate number of shares of common stock, par value $0.01 per share, issuable upon conversion of the 4.50% Senior Convertible Notes due 2025 for which the registrant will receive no additional consideration and for which no registration fee is payable pursuant to Rule 457(i) under the Securities Act. Pursuant to Rule 416 under the Securities Act, such number of shares of common stock registered hereby shall include an indeterminable number of shares of common stock that may be issued in connection with stock splits, stock dividends, recapitalization and similar events.

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PROSPECTUS SUPPLEMENT

(TO PROSPECTUS DATED JANUARY 28, 2019)

OPKO Health, Inc.

$200,000,000

4.50% Convertible Senior Notes due 2025

Interest payable on February 15 and August 15

We are offering $200,000,000 principal amount of our 4.50% Convertible Senior Notes due 2025 (the notes). The notes will bear interest at a rate of 4.50% per year, payable semiannually in arrears on February 15 and August 15 of each year, beginning on August 15, 2019. The notes will mature on February 15, 2025, unless earlier repurchased, redeemed or converted.

Holders may convert their notes at their option at any time prior to the close of business on the business day immediately preceding November 15, 2024 only under the following circumstances: (1) during any calendar quarter commencing after the calendar quarter ending on March 31, 2019 (and only during such calendar quarter), if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (2) during the five business day period after any five consecutive trading day period (the measurement period) in which the trading price (as defined below) per $1,000 principal amount of notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each such trading day; (3) if we call any or all of the notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date; or (4) upon the occurrence of specified corporate events. On or after November 15, 2024, until the close of business on the business day immediately preceding the maturity date, holders of the notes may convert their notes at any time, regardless of the foregoing circumstances. Upon conversion, we will pay or deliver, as the case may be, cash, shares of our common stock, or a combination of cash and shares of our common stock, at our election, as described in this prospectus supplement.

The conversion rate for the notes will initially be 236.7424 shares of common stock per $1,000 principal amount of notes (equivalent to an initial conversion price of approximately $4.22 per share of common stock). The conversion rate for the notes will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events described in this prospectus supplement that occur prior to the maturity date of the notes or if we deliver a notice of redemption, in certain circumstances we will increase the conversion rate of the notes for a holder who elects to convert its notes in connection with such a corporate event or notice of redemption as the case may be.

We may not redeem the notes prior to February 15, 2022. We may redeem for cash any or all of the notes, at our option, on or after February 15, 2022, if the last reported sale price of our common stock has been at least 130% of the conversion price for the notes then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. No sinking fund is provided for the notes.

If we undergo a fundamental change prior to the maturity date of the notes, holders may require us to repurchase for cash all or any portion of their notes at a repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. The notes will be our senior unsecured obligations and will rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the notes; equal in right of payment to any of our existing and future liabilities that are not so subordinated; effectively junior in right of payment to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our current or future subsidiaries.

Concurrently with this offering and by means of a separate prospectus supplement and accompanying prospectus, up to 30,000,000 of shares of our common stock will be offered by selling stockholders, who will borrow such shares through lending arrangements from an affiliate of the underwriter, which, as Share Borrower, is borrowing the shares from us. The borrowed shares are newly-issued shares issued in connection with this transaction and will be cancelled or held as treasury shares by us upon the expiration or the early termination of the share lending arrangements described herein. We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their investments in the notes. The selling stockholders may effect such transactions by selling the borrowed shares at various prices from time to time through the Share Borrower or its affiliates. The selling stockholders will receive all of the net proceeds from the sale of the borrowed shares, and we will not receive any of those proceeds, but we will receive from the Share Borrower a one-time nominal fee of $0.01 per share for each newly issued share. The concurrent offering of the borrowed shares is conditioned upon the closing of this offering.

Investing in the notes and our common stock involves risks. See Risk Factors beginning on page S-18 of this prospectus supplement, as well as the documents we file with the Securities and Exchange Commission that are incorporated by reference herein for more information.

PRICE: 100%, PLUS ACCRUED INTEREST, IF ANY

The notes are a new issue of securities with no established trading market. We do not currently intend to apply to list the notes on any securities exchange or any automated dealer quotation system. Our common stock is listed on the Nasdaq Global Select Market under the symbol OPK. The last reported sale price of our common stock on the Nasdaq Global Select Market on February 4, 2019 was $3.52 per share.

	Per Note	Total
Public Offering Price(1)	$ 1,000.00	$ 200,000,000.00
Underwriting Discounts	$ 35.00	$ 7,000,000.00
Proceeds to Us (before expenses)	$ 965.00	$ 193,000,000.00

(1) Plus accrued interest, if any, from February 7, 2019
If the underwriter sells more than the total principal amount of notes set forth above, the underwriter has an option, exercisable within a 30-day period, to purchase up to an additional $30,000,000 principal amount of notes from us solely to cover overallotments, if any.

Neither the U.S. Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

We expect that delivery of the notes will be made to investors in book-entry form through The Depository Trust Company on or about February 7, 2019. The issue price will include accrued interest, if any, from February 7, 2019 if settlement occurs after that date.

Sole Book-Running Manager

Jefferies

February 4, 2019

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Prospectus Supplement

Prospectus

We have not, and the underwriter has not, authorized anyone to provide any information or to make any representations other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus is an offer to sell only the notes offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of the respective dates of such documents.

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ABOUT THIS PROSPECTUS SUPPLEMENT

Unless the context otherwise requires, all references in this prospectus supplement to OPKO, Company, our company, we, us, or our refer to OPKO Health, Inc., a Delaware corporation, including its wholly-owned subsidiaries.

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the SEC) using a shelf registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part consists of the accompanying prospectus, which provides more general information, some of which may not apply to this offering. Generally, when we refer only to the prospectus, we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein.

This prospectus supplement and the accompanying prospectus relate to the offering of the notes. Before buying any notes offered hereby, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated herein and therein by reference as described under the headings Where You Can Find More Information and Incorporation of Certain Information by Reference. These documents contain important information that you should consider when making your investment decision.

You should rely only on the information contained in or incorporated by reference into this prospectus supplement, the accompanying prospectus and any free writing prospectus authorized by us. To the extent the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus or any document filed prior to the date of this prospectus supplement and incorporated by reference, the information in this prospectus supplement will control. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

The industry and market data and other statistical information contained in the documents we incorporate by reference are based on management s own estimates, independent publications, government publications, reports by market research firms or other published independent sources and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information.

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PROSPECTUS SUPPLEMENT SUMMARY

The following summary of our business highlights some of the information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. Because this is only a summary, however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, which are described under Incorporation of Certain Information by Reference in this prospectus supplement and in the accompanying prospectus. You should also carefully consider the matters discussed in the section in this prospectus supplement entitled Risk Factors and in the accompanying prospectus, in our Annual Report on Form 10-K for the year ended December 31, 2017 and in the other documents incorporated herein by reference.

Our Company

We are a diversified healthcare company that seeks to establish industry-leading positions in large and rapidly growing medical markets. Our diagnostics business includes BioReference Laboratories, the nation s third-largest clinical laboratory with a core genetic testing business and an almost 300-person sales and marketing team to drive growth and leverage new products, including the *4Kscore* prostate cancer diagnostic test and the *Claros 1* in-office immunoassay platform (in development). Our pharmaceutical business features *Rayaldee*, a U.S. Food and Drug Administration (FDA) approved treatment for secondary hyperparathyroidism in adults with stage 3 or 4 chronic kidney disease and vitamin D insufficiency (launched in November 2016), OPK88004, a selective androgen receptor modulator which we have studied for benign prostatic hyperplasia but for which we are exploring other potential indications, and OPK88003, a once or twice weekly oxyntomodulin for type 2 diabetes and obesity which is a clinically advanced drug candidate among the new class of GLP-1 glucagon receptor dual agonists (phase 2b). Our pharmaceutical business also features hGH-CTP, a once-weekly human growth hormone injection (in phase 3 and partnered with Pfizer Inc. (Pfizer)).

We operate established pharmaceutical business operations in Spain, Ireland, Chile and Mexico, which are generating revenue and from which we expect to generate positive cash flow and facilitate future market entry for our products currently in development. We have a development and commercial supply pharmaceutical company, as well as a global supply chain operation and holding company in Ireland, which we expect will play an important role in the development, manufacturing, distribution and approval of a wide variety of drugs with an emphasis on high potency products. We also own a specialty active pharmaceutical ingredients manufacturer in Israel, which we expect will facilitate the development of our pipeline of molecules and compounds for our proprietary molecular diagnostic and therapeutic products.

We are a Delaware corporation. We maintain our principal executive offices at 4400 Biscayne Blvd., Miami, FL 33137. Our telephone number is (305) 575-4100. We maintain a website at *www.opko.com*. The information contained on our website or that can be accessed through our website does not constitute part of this prospectus supplement or the accompanying prospectus.

Current Products and Services and Related Markets

Diagnostics

BioReference Laboratories

Through BioReference, the third largest full service clinical laboratory in the U.S., we offer comprehensive laboratory testing services utilized by healthcare providers in the detection, diagnosis, evaluation, monitoring and treatment of

diseases, including esoteric testing, molecular diagnostics, anatomical pathology, genetics, women s

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health and correctional healthcare. We market and sell these services to physician offices, clinics, hospitals, employers and governmental units nationally, with the largest concentration of business in the larger metropolitan areas across New York, New Jersey, Florida, Texas, Maryland, California, Pennsylvania, Delaware, Washington DC, Illinois and Massachusetts.

BioReference has an almost 300-person sales and marketing team and operates a network of approximately 200 patient service centers.

Our BioReference laboratory testing business consists of routine testing and esoteric testing. Routine tests measure various health parameters, such as the functions of the heart, kidney, liver, thyroid and other organs, including such tests as blood cell counts, cholesterol levels, pregnancy, substance abuse and urinalysis. We typically operate 24 hours per day, 365 days per year and perform and report most routine test results within 24 hours.

The esoteric tests we perform require sophisticated equipment and materials, highly skilled personnel and professional attention. Esoteric tests are ordered less frequently than routine tests and typically are priced higher than routine tests. Esoteric tests include tests related to endocrinology, genetics and genomics, immunology, microbiology, HIV tests, molecular diagnostics, next generation sequencing, oncology, serology and toxicology.

Through BioReference, we operate in the following highly specialized laboratory divisions:

BioReference Laboratories. BioReference constitutes our core clinical testing laboratory offering automated, high volume routine testing services, STAT testing, informatics, HIV, Hep C and other molecular tests.

GenPath (Oncology). National oncology presence with expertise in cancer pathology and diagnostics, as well as molecular diagnostics. Core tests include FLOW, IHC, MicroArray, FISH, ISH, Morphology and full-service oncology.

GenPath (Women s Health). Innovative technology platform for sexually transmitted infections has enabled expansion nationally with specimens coming from 41 states, including Image Directed Paps analysis, HPV Plus and STI Testing.

GeneDx. Industry leading national laboratory for testing rare and ultra-rare genetic diseases with international reach, performing testing on specimens from more than 50 countries.

Laboratorio Bueno Salud. National testing laboratory dedicated to serving the Spanish-speaking population in the U.S., where all business is conducted in Spanish including patient and physician interaction.

We have one of the largest marketing staffs of any laboratory in the country with sales and marketing groups dedicated to urology, oncology, women s health, genetic testing and correctional health, as well as cross-over groups selling to large institutions. All of our sales and marketing personnel operate in a dual capacity, as both marketing and client support representatives, which we believe provides better customer service and a strong connection with our customers.

We expect the clinical laboratory testing industry will continue to experience growth in testing volumes due to aging of the population in the U.S., patient awareness of the value of laboratory tests, a decrease in the cost of tests, the development of sophisticated and specialized tests for detection and management of disease, increased recognition of early detection and prevention as a means of reducing healthcare costs and ongoing research and development in genetics and genomics and personalized medicine. Our mission is to be recognized by our clients as the premier provider of clinical laboratory testing, information and related services.

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BioReference provides us with a significant diagnostics commercial infrastructure for marketing and sales that reached almost 11 million patients in 2018. In addition, its large team of managed care experts complement our efforts to ensure that payors recognize the value of our diagnostic and laboratory tests for reimbursement purposes. We continue to leverage the national marketing, sales and distribution resources of BioReference, along with its almost 300-person sales and marketing team, to enhance sales of and reimbursement for our 4Kscore test, a laboratory developed blood test that provides a personalized risk score for aggressive prostate cancer. We plan to continue to leverage the BioReference commercial infrastructure and capabilities, as well as its extensive relationships with payors, to commercialize OPKO s other diagnostic products under development, including the *Claros 1*.

4Kscore Test

We offer the *4Kscore* test through our BioReference laboratory located in Elmwood Park, New Jersey. We began selling the *4Kscore* test in the U.S. in March 2014 and in Europe and Mexico in September 2014 and January 2015, respectively. The *4Kscore* test is a laboratory developed test that measures the blood plasma levels of four different prostate-derived kallikrein proteins: Total PSA, Free PSA, Intact PSA and Human Kallikrein-2 (hK2). These biomarkers are then combined with a patient s age, Digital Rectal Exam (DRE) status (nodule / no nodule), and prior negative biopsy status (yes / no) using a proprietary algorithm to calculate the risk (probability) of finding a Gleason Score 7 or higher prostate cancer. The four kallikrein panel of biomarkers utilized in the *4Kscore* test is based on decades of research conducted by scientists at Memorial Sloan-Kettering Cancer Center and leading European institutions. Investigators at the Lund University, Sweden, University of Turku, Finland and Memorial Sloan Kettering Cancer Center, New York, have also demonstrated that the *4Kscore* test can risk stratify the 20-year risk for development of prostate metastases and mortality in men who present at age 50 or 60 years old with an elevated PSA.

The *4Kscore* test was developed by OPKO and validated in two prospective, blinded studies of 1,012 and 366 men, respectively. The first study was done in collaboration with 26 urology centers across the U.S. and the second study was conducted at eight VA centers in the U.S. with a predominantly African American cohort. African Americans are 1.7 times more likely to be diagnosed with prostate cancer than Caucasian men and 2.2 times more likely to die from the disease. Results showed that the *4Kscore* test was highly accurate for predicting the presence of high-grade cancer (Gleason score 7 or higher) prior to prostate biopsy, regardless of race. The full data from the blinded, prospective U.S. clinical validation studies have been published in peer reviewed medical journals.

The clinical data from both studies demonstrated the ability of the *4Kscore* test to discriminate between men with high-grade, aggressive prostate cancer and those men who had no findings of cancer or had low-grade or indolent form of the disease. The discrimination, measured by Area Under the Curve (AUC) analysis, was greater than 0.80 and is significantly higher than previously developed tests. Furthermore, the *4Kscore* test demonstrated excellent risk calibration, indicating the accuracy of the result for an individual patient, both Caucasian and African American. The high value of AUC and the excellent risk calibration make the *4Kscore* test result valuable information for the shared decision-making between the urologist and patient on whether or not to perform a prostate biopsy.

A separate clinical utility study indicated that the *4Kscore* test led to 64.6% fewer biopsies. The study, The *4Kscore*® Test Reduces Prostate Biopsy Rates in Community and Academic Urology Practices , was published in a peer reviewed medical journal. The study, which included 611 patients seen by 35 academic and community urologists across the U.S., evaluated the influence of the *4Kscore* test on urologist- patient decisions about whether to perform a biopsy in men who had an abnormal PSA and or DRE result. Test results for patients were stratified into low risk (< 7.5%), intermediate risk (7.5%-19.9%) and high risk (³20%) for developing aggressive prostate cancer. Nearly half (49.3%) of the men were categorized as low risk; 25.7% and 25.0% fell into the

intermediate-risk and high-risk categories, respectively. Notably, the *4Kscore* test results influenced biopsy decisions in 88.7% of the men. In the three risk groups, a biopsy was avoided in 94.0%, 52.9% and 19.0% of men in the low, intermediate and high-risk categories, respectively.

The *4Kscore* test has been granted a Category I CPT® code by the AMA (CPT Code 81539). A CPT code is used by insurance companies and government payors to describe health care services and procedures. A Category I CPT code is critical to facilitate reimbursement in government programs such as Medicare and Medicaid, as well as private insurance programs.

The National Comprehensive Cancer Network (NCCN) included the *4Kscore* test as a recommended test in their 2015, 2016, 2017 and 2018 Guidelines for Prostate Cancer Early Detection. The panel making this recommendation concluded that the *4Kscore* test is indicated for use prior to a first prostate biopsy, or after a negative biopsy, to assist patients and physicians in further defining the probability of high-grade cancer. In addition, the European Association of Urology (EAU) Prostate Cancer Guidelines Panel included the *4Kscore* test in the 2018 EAU Guidelines for Prostate Cancer, concluding that the *4Kscore*, as a blood test with greater specificity over the PSA test, is indicated for use prior to a first prostate biopsy or after a negative biopsy to assist patients and physicians in further defining the probability of high-grade cancer.

We have and will continue to commit substantial efforts to obtaining broad reimbursement coverage for the *4Kscore* test. We have obtained a positive coverage decision from at least one national private payor and pricing agreements from several regional payors. Novitas Solutions, the local Medicare Administrative Contractor (MAC) for our laboratory in New Jersey, issued a proposed non-coverage policy for the *4Kscore* test in May 2018 subject to a public comment period ending July 5, 2018. We made oral presentations at a Novitas open meeting and submitted substantial evidence and data to address the comments raised in the draft non-coverage determination. In January 2019, Novitas issued a notice of a future non-coverage determination for the 4*KScore* test to be effective March 20, 2019. We are evaluating options to appeal the decision and undertake other steps with the Center for Medicare and Medicaid Services (CMS) in an effort to have this determination rescinded or reversed.

Point-of-Care Diagnostics

OPKO Diagnostics, LLC (OPKO Diagnostics), formerly Claros Diagnostics, Inc., has developed a novel diagnostic instrument system to provide rapid, high performance blood test results in the point-of-care setting. The technology only requires a finger stick drop of blood introduced into the test cassette that can then run a quantitative test. The instrument performs the tests on a disposable, one-time usable cassette that is a microfluidics-based diagnostic test system. The credit card-sized test cassette works with a sophisticated desktop analyzer to provide high performance quantitative blood test results within minutes and permits the transition of complex immunoassays from the centralized reference laboratory to the physician s office, hospital nurses station or other decentralized location.

We completed multiple in vitro analytical validation and field use tests for the PSA test in mid-2017 and filed the pre-marketing authorization (PMA) for the Claros Analyzer and Sangia Total PSA Test with the FDA in November 2017. The key clinical study with patients who were suspicious for prostate cancer found that the Sangia Total PSA test improved the sensitivity of a DRE to 91%, detecting 2.9 times the prostate cancers compared to DRE alone. The FDA approved the PMA for the Sangia Total PSA Test using the Claros Analyzer in January 2019. We also intend to commence a clinical trial of a testosterone diagnostic test for our point-of-care system. We expect to fully leverage BioReference s marketing, sales and distribution resources for the launch of the *Claros 1* system and associated diagnostic tests in the U.S.

We are also presently working to add additional tests for our point-of-care system, including parathyroid hormone (PTH) and vitamin D, and we believe that there are many more applications for the technology, including infectious disease, cardiology, women s health and companion diagnostics.

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Pharmaceutical Business

We currently have one commercial stage pharmaceutical product and several pharmaceutical compounds and technologies in various stages of research and development for a broad range of indications and conditions, including the following:

Renal Products

We launched *Rayaldee*, our lead renal product, in the U.S. market in November 2016. In June 2016, the FDA approved *Rayaldee* extended release capsules for the treatment of secondary hyperparathyroidism (SHPT) in adults with stage 3 or 4 chronic kidney disease (CKD) and vitamin D insufficiency, defined as serum total 25-hydroxyvitamin D levels less than 30 ng/mL. *Rayaldee* is a patented extended release product containing 30 mcg of a prohormone called calcifediol (25-hydroxyvitamin D3).

We have a 79-person highly specialized sales, marketing and market access team dedicated to the launch and commercialization of *Rayaldee* as of December 31, 2018. As compared to the fourth quarter of 2017 and the third quarter of 2018, total *Rayaldee* prescriptions increased approximately 141% and 17%, respectively, in the fourth quarter of 2018. Efforts are underway to obtain broader commercial and Part D insurance coverage for *Rayaldee*. We have already contracted for commercial and Part D coverage for more than seventy percent (70%) of U.S. covered lives as of the end of 2018.

In connection with the launch of *Rayaldee*, we have also engaged in a comprehensive ongoing market education campaign highlighting the unmet need in treating SHPT, including by leveraging key opinion leaders in community outreach programs such as speakers bureaus and patient advocacy programs.

In May 2016, we entered into a collaboration with Vifor Fresenius Medical Care Renal Pharma (VFMCRP) for the development and commercialization of *Rayaldee* in Europe, Canada, Mexico, Australia, South Korea and certain other international markets for the treatment of SHPT in patients with stage 3, 4 or 5 CKD and vitamin D insufficiency. Under the terms of the agreement, OPKO received an upfront payment of $50 million. We also received a $2 million payment triggered by the marketing approval of *Rayaldee* in Canada and will receive up to $230 million in additional regulatory and sales-based milestones. In addition, VFMCRP will pay OPKO tiered, double digit royalties on sales of the product at percentage rates that range from the mid-teens to the mid-twenties or a minimum royalty, whichever is greater, upon commencement of sales of the product. OPKO and VFMCRP are also collaborating to develop and commercialize a new dosage form of *Rayaldee* for the treatment of SHPT in hemodialysis patients. OPKO granted VFMCRP an option to acquire rights to this dosage form for the U.S. market; if exercised, OPKO will receive up to $555 million in additional milestones and double digit royalties.

On October 12, 2017, we entered into a Development and License Agreement (the JT Agreement) with Japan Tobacco Inc. (JT) granting JT the exclusive rights for the development and commercialization of *Rayaldee* in Japan (the JT Territory). The license grant to JT covers the therapeutic and preventative use of the product for (i) SHPT in non-dialysis and dialysis patients with CKD, (ii) rickets, and (iii) osteomalacia, as well as such additional indications as may be added to the scope of the license subject to the terms of the JT Agreement. Under the terms of the JT Agreement, OPKO received an initial upfront payment of $6 million and we received another $6 million milestone payment triggered by the initiation of OPKO s U.S. phase 2 study with *Rayaldee* in dialysis patients. OPKO is also eligible to receive up to an additional aggregate amount of $31 million upon the achievement of certain regulatory and development milestones by JT for *Rayaldee* in the JT Territory, and $75 million upon the achievement of certain sales based milestones by JT in the JT Territory. OPKO will also receive tiered, double digit royalty payments at rates ranging from low double digits to mid-teens on net product sales within the JT Territory. JT will, at its sole cost and

expense, be responsible for performing all development

activities necessary to obtain all regulatory approvals for *Rayaldee* in Japan and for all commercial activities pertaining to *Rayaldee* in Japan, except for certain preclinical expenses which OPKO has agreed to reimburse JT up to a capped amount.

The FDA approval of *Rayaldee* was supported by successful results from two identical randomized, double-blind, placebo-controlled, multi-site phase 3 studies which established the safety and efficacy of *Rayaldee* as a new treatment for SHPT in adults with stage 3 or 4 CKD and vitamin D insufficiency.

Vitamin D insufficiency arises in CKD due to the abnormal upregulation of CYP24A1, an enzyme that destroys vitamin D and its metabolites, and from many other causes as well.

Studies in CKD patients have demonstrated that currently available over-the-counter and prescription vitamin D supplements cannot reliably raise blood vitamin D prohormone levels and effectively treat SHPT, a condition commonly associated with CKD in which the parathyroid glands secrete excessive amounts of PTH. Prolonged elevation of blood PTH causes excessive calcium and phosphorus to be released from bone, leading to elevated serum calcium and phosphorus levels, softening of the bones (osteomalacia) and calcification of vascular and renal tissues. SHPT affects 40-82% of patients with stage 3 or 4 CKD and approximately 95% of patients with stage 5 CKD.

The completed phase 3 trials for *Rayaldee* successfully met all primary efficacy and safety endpoints. The primary efficacy endpoint was a responder analysis in which responder was defined as any treated subject who demonstrated an average decrease in PTH of at least 30% from pre-treatment baseline during the last six weeks of the 26-week treatment period. A significantly higher response rate was observed with *Rayaldee* compared to placebo treatment in both trials and safety and tolerability data were comparable in both treatment groups. The PTH-lowering response rates with *Rayaldee* were similar in both stage 3 and 4 CKD. Patients completing the two pivotal trials were treated, at their election, for an additional six months with *Rayaldee* during an open-label extension study. Data from the extension study indicated that the PTH lowering response rate steadily increased with duration of *Rayaldee* treatment without deterioration in safety profile.

We also are developing *Rayaldee* for other indications, including for SHPT in patients with vitamin D insufficiency and stage 5 CKD requiring regular hemodialysis. A phase 2 study of a higher dose product commenced in this patient population during the third quarter of 2018. We expect to receive data from the study in the second half of 2020.

In August 2014, we also announced the submission of an Investigational New Drug Application (IND) to the FDA to evaluate *Rayaldee* as an adjunctive therapy for the prevention of skeletal-related events in patients with bone metastases undergoing anti-resorptive therapy. We commenced a phase 1 dose escalation study in the fourth quarter of 2014 in breast and prostate cancer patients with bone metastases who were receiving anti-resorptive therapy. The study, which has been completed, was designed to evaluate safety, markers of vitamin D and mineral metabolism and tumor progression. We are currently collecting the final data and will shortly complete a final analysis of the study.

We filed an IND for *Rayaldee* in January 2019 for the treatment of SHPT arising from vitamin D insufficiency in patients who have undergone bariatric surgery. We intend to commence a phase 2 study in this population in the first half of 2019.

Our second most advanced renal product, Alpharen (Fermagate Tablets), is a new and potent non-absorbed phosphate binder to treat hyperphosphatemia in stage 5 CKD patients requiring regular hemodialysis. Alpharen (Fermagate Tablets) has been shown to be safe and effective in treating hyperphosphatemia in phase 2 and 3 trials in stage 5 CKD patients undergoing chronic hemodialysis. Hyperphosphatemia, or elevated serum phosphorus, is common in dialysis patients and tightly linked to the progression of SHPT and vascular

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calcification, both of which drive morbidity and mortality. The kidneys provide the primary route of excretion for excess phosphorus absorbed from ingested food. As kidney function worsens, serum phosphorus levels increase and directly stimulate PTH secretion. Stage 5 CKD patients requiring dialysis must reduce their dietary phosphate intake and usually require regular treatment with orally administered phosphate binding agents to lower serum phosphorus to meet the recommendations of the Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guidelines that elevated serum phosphorus levels should be lowered. Hyperphosphatemia contributes to soft tissue mineralization and affects approximately 90% of dialysis patients. Dialysis patients require ongoing phosphate binder treatment to maintain controlled serum phosphorus levels. A single additional phase 3 clinical trial is required to support marketing approvals for Alpharen in North America and in Europe.

We believe the CKD patient population is large and growing as a result of obesity, hypertension and diabetes; therefore this patient population represents a significant global market opportunity. According to the National Kidney Foundation, CKD afflicts over 40 million people in the U.S., including more than 21 million patients with stage 3 or 4 CKD. In stage 5 CKD, kidney function is minimal to absent and most patients require regular dialysis or a kidney transplant for survival. An estimated 71-97% of CKD patients have vitamin D insufficiency which can lead to SHPT and its debilitating consequences. CKD continues to be associated with poor outcomes, reflecting the inadequacies of the current standard of care.

Vitamin D insufficiency, hyperphosphatemia and SHPT, when inadequately treated, are major contributors to poor CKD outcomes. We intend to develop and commercialize *Rayaldee* and Alpharen to constitute part of the foundation for a new and markedly improved standard of care for CKD patients having SHPT and/or hyperphosphatemia.

SARM

Through the acquisition of Transition Therapeutics, a Toronto-based biotechnology company (Transition), we acquired OPK88004, an orally administered selective androgen receptor modulator (SARM) which we have been developing for the treatment of Benign Prostatic Hypertrophy (BPH) and other urologic and metabolic conditions. The selective and antagonistic properties of OPK88004 on the prostate appear to be well suited to potentially reduce prostate hyperplasia and volume, as well as provide anabolic therapeutic benefits such as increased lean body mass and physical function, and decreased fat mass in specific patient populations. We believe that SARMs hold considerable promise as new class of anabolic therapies for a variety of clinical indications, such as frailty and functional limitations associated with aging and chronic illnesses, cancer and osteoporosis.

A phase 2 study of 350 male subjects for another indication showed significantly increased lean body mass and muscle strength and significant fat mass reduction with no change in lower PSA levels. OPK88004 is currently being studied in a phase 2 study in prostate cancer patients who have undergone radical prostatectomy. The main objective of the study is to examine the effect of OPK88004 on sexual function and quality of life issues associated with this patient population. An additional phase 2b study to determine the optimal dose to treat patients with BPH commenced in November 2017 and we completed enrollment and randomized 114 patients in the U.S. in December 2018. The main focus of the study is to determine the optimal dose of OPK88004 that will reduce prostate volume and PSA levels, and increase anabolic effects such as lean body and decreased fat mass in BPH patients. Blinded data from the phase 2b study have shown significant variability in the measurement of prostate volume, rendering the assessment of prostate volume from treatment impractical. Additionally, a small number of subjects have shown increased liver enzymes. We plan to suspend the current trial but continue to analyze data relating to the study s other primary endpoint, the effect of OPK88004 on serum PSA levels, and the secondary endpoints, changes in lean body mass and fat mass. The results of this data analysis are expected in the second quarter of 2019. Additional indications including treatment of symptoms associated with androgen deprivation therapy in prostate cancer patients and low testosterone levels, muscle weakness and general frailty in kidney dialysis patients are being planned.

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Oxyntomodulin

Our internal product development program is also currently focused on developing a once weekly administered oxyntomodulin for type 2 diabetes and obesity. Our most advanced oxyntomodulin product candidate, OPK88003, a once-weekly administered peptide for the treatment of type 2 diabetes and associated obesity, is a dual agonist of the Glucagon-Like Peptide-1 (GLP-1) and glucagon receptors. The receptors play an integral role in regulating appetite, food intake, satiety and energy utilization in the body. Stimulating both of the receptors, OPK88003 has the potential to regulate blood glucose.

OPK88003 has been evaluated in a phase 2 study enrolling 420 type 2 diabetes subjects in a 24-week study consisting of a 12-week randomized blinded stage followed by a 12-week open-label stage. The study included four once-weekly dose arms of OPK88003 (10mg, 15mg, 30mg, 50mg), a placebo arm and an active comparator arm (exenatide extended release 2mg). The study was completed in February 2016.

Subjects receiving the highest dose of OPK88003 peptide once weekly in the study demonstrated significantly superior weight loss compared with currently approved extended release exenatide and placebo after 12 and 24 weeks of treatment. OPK88003 also provided a reduction in HbA1c, a marker of sugar metabolism, similar to exenatide at weeks 12 and 24.

OPK88003 is currently being evaluated in a dose escalation phase 2b trial in 110 type 2 diabetics in which patients are treated with a dose escalation regimen over 3 months intended to optimize dose levels, and increase body weight loss and reduce the adverse event profile, such as nausea and vomiting. Patient enrollment was completed in June 2018. The patients will be treated for a total of 30 weeks in the study. We expect to receive data from the study in the first quarter of 2019. The key primary endpoint will be HbA1c and secondary endpoints such as weight loss, lipid profile and safety will also be analyzed.

We believe oxyntomodulin has potential to be a safe, long term therapy for obesity and diabetes type II patients, representing significant market opportunities. More than 380 million are living with diabetes worldwide, of which approximately 90% have type II diabetes. According to the World Health Organization, there are more than 500 million severely overweight or obese people.

Biologics

Our biologics business focuses on developing and commercializing longer-acting proprietary versions of already approved therapeutic proteins. One of our innovative platform technologies uses a short, naturally-occurring amino acid sequence, carboxl terminal peptide (CTP), which has the effect of slowing the removal from the body of the therapeutic protein to which it is attached. This CTP can be readily attached to a wide array of existing therapeutic proteins, stabilizing the therapeutic protein in the bloodstream and extending its life span without additional toxicity or loss of desired biological activity. We are using the CTP technology to develop new, proprietary versions of certain existing therapeutic proteins that have longer life spans than therapeutic proteins without CTP. We believe that our products will have greatly improved therapeutic profiles and distinct market advantages.

hGH-CTP

Our lead product candidate utilizing CTP, hGH-CTP, is a recombinant human growth hormone product under development for the treatment of growth hormone deficiency (GHD), which is a pituitary disorder resulting in short stature in children and other physical ailments in both children and adults.

In December 2014, we entered into an exclusive worldwide agreement with Pfizer for the development and commercialization of hGH-CTP for the treatment of GHD in adults (Adult GHD) and in children (Pediatric

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GHD), as well as for the treatment of growth failure in children born small for gestational age (SGA). In connection with the transaction, we granted Pfizer an exclusive license to commercialize hGH-CTP worldwide, and we received non-refundable and non-creditable upfront payments of $295 million and are eligible to receive up to an additional $275 million upon the achievement of certain regulatory milestones. In addition, we are eligible to receive initial tiered royalty payments associated with the commercialization of hGH-CTP for Adult GHD with percentage rates ranging from the high teens to mid-twenties. Upon the launch of hGH-CTP for Pediatric GHD in certain major markets, the royalties will transition to regional, tiered gross profit sharing for both hGH-CTP and Pfizer s Genotropin®.

Pursuant to our agreement with Pfizer, we will lead the clinical development activities for the hGH-CTP program and will be responsible for funding the development programs for the key indications, which includes Adult and Pediatric GHD and Pediatric SGA. Pfizer will be responsible for all development costs for additional indications as well as all post-marketing studies. In addition, Pfizer will fund the commercialization activities for all indications and lead the manufacturing activities covered by the global development plan.

GHD occurs when the production of growth hormone, secreted by the pituitary gland, is disrupted. Since growth hormone plays a critical role in stimulating body growth and development, and is involved in the production of muscle protein and in the breakdown of fats, a decrease in the hormone affects numerous body processes. hGH is used for the long-term treatment of children and adults with inadequate secretion of endogenous growth hormone. The primary indications it treats in children are GHD, SGA, kidney disease, Prader-Willi Syndrome and Turner s Syndrome. In adults, the primary indications are replacement of endogenous growth hormone and the treatment of AIDS-induced weight loss. Patients using hGH receive daily injections six or seven times a week. This is particularly burdensome for pediatric patients. We believe a significant market opportunity exists for a longer-lasting version of hGH that would require fewer injections.

Our phase 3 trial of hGH-CTP in pediatric patients was initiated in December 2016 and patient enrollment was completed in August 2018. The global study is a 225-patient study in Pediatric GHD patients designed to evaluate weekly treatment with hGH-CTP versus daily injections of Genotropin. The hGH-CTP is delivered in a pen device in this multi-regional study in over 21 countries. The GHD subjects will be treated weekly for 12 months. We expect to perform top-line data analysis from the study in the fourth quarter of 2019. In addition to the phase 3 pediatric study, we have continued without interruption our ongoing phase 2 pediatric open label extension study for hGH-CTP. The phase 2 pediatric patients have been treated with hGH-CTP for over four years, and some patients for over five years. We have switched all of the pediatric patients in this study to the disposable pen device. We have also initiated a 44-patient study in Pediatric GHD patients in Japan which is nearing completion of enrollment. hGH-CTP has orphan drug designation in the U.S. and Europe for both adults and children with GHD.

In December 2016, we announced preliminary topline data from our phase 3, double blind, placebo controlled study of hGH-CTP in adults with GHD. The multinational, multi-center study, which utilized a 2:1 randomization between hGH-CTP and placebo, enrolled 203 subjects, 198 of whom received at least one dose of study treatment. Treatment was administered through a weekly injection. The topline results showed:

The active group had a mean change in trunk fat mass of -0.4kg and placebo group was 0;

There was no statistically significant difference (£ 0.05 (p value)) between the active and placebo group;

97% of hGH-CTP vs 6% of placebo group showed IGF-1 normalization; and

The safety profile of hGH-CTP is consistent with that observed with those treated with daily growth hormone.

Although there was no statistically significant difference between hGH-CTP and placebo on the primary endpoint of change in trunk fat mass from baseline to 26 weeks, after unblinding the study, we identified an

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exceptional value of trunk fat mass reduction in the placebo group that may have affected the primary outcome. We have completed post-hoc sensitivity analyses to evaluate the influence of outliers on the primary endpoint results using multiple statistical approaches. Analyses that excluded outliers showed a statistically significant difference between hGH-CTP and placebo on the change in trunk fat mass. Additional analyses that did not exclude outliers showed mixed results. Following completion of the analyses, OPKO and Pfizer have agreed that OPKO may communicate with the FDA regarding a potential biologics license application (BLA) submission.

Factor VII

In addition to hGH-CTP, we are developing a product to extend the life span of Factor VIIa (hemophilia) using the CTP technology. In February 2013, the FDA granted orphan drug designation to our longer-acting version of clotting Factor VIIa, Factor VIIa-CTP, for the treatment of bleeding episodes in patients with hemophilia A or B with inhibitors to Factor VIII or Factor IX. Currently, Factor VIIa therapy is available only as an intravenous (IV) formulation which, due to Factor VIIa s short half-life, requires multiple infusions to treat a bleeding episode. In addition, frequent infusions are onerous when used as preventative prophylactic therapy, especially for children.

We have conducted a phase 1/2a dose escalation study and a phase 1 dose escalating subcutaneous study in healthy volunteers to determine safety of our long acting Factor VIIa-CTP for the treatment of bleeding episodes in hemophilia A or B patients with inhibitors to Factor VIII or Factor IX. These two studies are completed, and data assessment is on-going. Further regulatory and development strategies will be planned.

We believe that the CTP technology may also be broadly applicable to other therapeutic proteins in the market and provide a reduction in the number of injections.

APIs

FineTech Pharmaceutical, Ltd. (FineTech) is our Israeli-based subsidiary that develops and produces high value, high potency specialty APIs. Through its FDA registered facility in Nesher, Israel, FineTech currently manufactures commercial APIs for sale or license to pharmaceutical companies in the U.S., Canada, Europe and Israel. We believe that FineTech s significant know-how and experience with analytical chemistry and organic syntheses, together with its production capabilities, may play a valuable role in the development of our pipeline of proprietary molecules and compounds for diagnostic and therapeutic products, while providing revenues and profits from its existing API business.

Oligonucleotide Therapeutics

OPKO CURNA, LLC (CURNA), previously CURNA Inc., is engaged in the discovery of new drugs for the treatment of a wide variety of illnesses, including cancer, heart disease, metabolic disorders and a range of genetic anomalies. CURNA s platform technology utilizes a short, single strand oligonucleotide and is based on the up-regulation of protein production through interference with non-coding RNA s or natural antisense. This strategy contrasts with established approaches which down-regulate protein production. CURNA has designed a novel type of therapeutic modality, termed AntagoNAT, and has initially demonstrated this approach for up-regulation of several therapeutically relevant proteins in *in vitro* and animal models.

CURNA has identified and developed potential active compounds which increase the production of over 80 key proteins involved in a large number of individual diseases. We have ongoing pre-clinical studies for several of these compounds. A lead compound has been identified for the treatment of Dravet Syndrome. Orphan disease designations are granted by FDA and EMA.

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NK-1 Program

We acquired rolapitant and other neurokinin-1 (NK-1) assets from Merck & Co. In December 2010, we exclusively out-licensed the development, manufacture and commercialization of our lead NK-1 candidate, VARUBI (rolapitant), to TESARO, Inc. (TESARO). VARUBI , a potent and selective competitive antagonist of the NK-1 receptor, had successfully completed clinical testing for prevention of chemotherapy induced nausea and vomiting (CINV) and post-operative induced nausea and vomiting. TESARO s NDA for oral VARUBI was approved by the FDA in September 2015, and in November 2015, TESARO commenced the commercial launch of oral VARUBI in the U.S. TESARO s IV formulation of VARUBI was approved by the FDA in October 2017 and commercial sales commenced in November 2017. In January 2018, the package insert for VARUBI was updated to include mention of new adverse effects, including anaphylaxis, anaphylactic shock and other serious hypersensitivity reactions which were reported following its introduction to the market in November 2017. In late February 2018, TESARO announced it would suspend distribution of VARUBI IV, but would continue to support the oral product.

Under the terms of the license, we received a $6.0 million upfront payment from TESARO and we received $30.0 million of milestone payments upon achievement of certain regulatory and commercial sale milestones. We are eligible to receive additional commercial milestone payments of up to $85.0 million if specified levels of annual net sales are achieved. TESARO is also obligated to pay us tiered royalties on annual net sales achieved in the U.S. and Europe at percentage rates that range from the low double digits to the low twenties, and outside of the U.S. and Europe at low double-digit percentage rates. TESARO assumed responsibility for clinical development and commercialization of licensed products at its expense. Under the agreement, we will continue to receive royalties on a county-by-country and product-by-product basis until the later of the date that all of the patents rights licensed from us and covering rolapitant expire, are invalidated or are not enforceable, and 12 years from the date of the first commercial sale of the product.

If TESARO elects to develop and commercialize VARUBI in Japan through a third-party licensee, TESARO will share equally with us all amounts it receives in connection with such activities, subject to certain exceptions and deductions. The term of the license will remain in force until the expiration of the royalty term unless we terminate the license earlier for TESARO s material breach of the license or bankruptcy. TESARO has a right to terminate the license during the term for any reason on three month s written notice. TESARO assigned its rights and obligations under the agreement to TerSera Therapeutics LLC (TerSera) in June 2018 pursuant to an asset purchase agreement. Under the asset purchase agreement, TerSera is responsible for VARUBI in the United States and Canada and TESARO can continue to commercialize VARUBY® in Europe and the rest of the world though a sublicense with TerSera.

Commercial Operations

We also intend to continue to leverage our global commercialization expertise to pursue acquisitions of commercial businesses that will both drive our growth and provide geographically diverse sales and distribution opportunities. During 2015, we acquired EirGen Pharma Ltd. (EirGen), a specialty pharmaceutical company based in Ireland. EirGen is focused on the development and commercial supply of high potency, high barrier to entry, pharmaceutical products. Through its facility in Waterford, Ireland, EirGen currently manufactures high potency pharmaceutical products and exports to over 50 countries. High potency drugs such as those used for cancer chemotherapy are typically unsuitable for manufacture in normal multi-product facilities due to cross contamination risks.

To date, EirGen and its commercial partners have filed several product applications with the FDA in Europe and in Japan. EirGen has a strong research and development portfolio of high barrier to entry drugs and we expect to rapidly expand its drug portfolio. We believe EirGen will play an important role in the development, manufacturing,

distribution and approval of a wide variety of drugs in a variety of dosage forms with an emphasis on high potency products.

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OPKO Health Europe (previously Farmadiet Group Holding, S.L.) operates primarily in Spain and has more than 20 years of experience in the development, manufacture, marketing and sale of pharmaceutical, nutraceutical and veterinary products in Europe.

OPKO Mexico (previously Pharmacos Exakta S.A. de C.V.), is engaged in the manufacture, marketing, sale and distribution of ophthalmic and other pharmaceutical products to private and public customers in Mexico. OPKO Mexico is commercializing food supplements and over the counter products, and manufactures and sells products primarily in the generics market in Mexico, although it also has some proprietary products as well.

OPKO Chile (previously Pharma Genexx, S.A.) markets, sells and distributes pharmaceutical products to the private, hospital, pharmacy and public institutional markets in Chile for a wide range of indications, including, cardiovascular products, vaccines, antibiotics, gastro- intestinal products and hormones, among others. ALS Distribuidora Limitada (ALS) is engaged in the business of importation, commercialization and distribution of pharmaceutical products for private markets in Chile. ALS started operations in 2009 as the exclusive product distributor of Arama Laboratorios y Compañía Limitada (Arama), a company with more than 20 years of experience in the pharmaceutical products market. In connection with the acquisition of ALS, OPKO acquired all of the product registrations and trademarks previously owned by Arama, as well as the Arama name. We distribute food supplements and over the counter products through Arama.

Strategic Investments

We have and may continue to make investments in other early stage companies that we perceive to have valuable proprietary technology and significant potential to create value for OPKO as a shareholder.

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The Offering

The summary below describes the principal terms of the notes. Certain of the terms and conditions described below are subject to important limitations and exceptions. A more detailed description of the terms and conditions of the notes is contained under the heading Description of Notes in this prospectus supplement. As used in this section, we, our and us refer to OPKO Health, Inc. and not to its consolidated subsidiaries.

Issuer	OPKO Health, Inc., a Delaware corporation.
Securities	$200,000,000 principal amount of 4.50% Convertible Senior Notes due 2025 (the notes) (or $230,000,000 if the underwriter exercises its overallotment option to purchase additional notes in full).
Maturity	February 15, 2025, unless earlier repurchased, redeemed or converted.
Interest	4.50% per year. Interest will accrue from February 7, 2019 and will be payable semiannually in arrears on February 15 and August 15 of each year, beginning on August 15, 2019.
Conversion Rights	Holders may convert their notes at their option prior to the close of business on the business day immediately preceding November 15, 2024, in multiples of $1,000 principal amount, only under the following circumstances: during any calendar quarter commencing after the calendar quarter ending on March 31, 2019 (and only during such calendar quarter), if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; during the five business day period after any five consecutive trading day period (the measurement period) in which the trading price (as defined under Description of Notes Conversion Rights Conversion upon Satisfaction of Trading Price Condition) per $1,000 principal amount of notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our common stock and the conversion rate on

each such trading day;

if we call the notes for redemption, at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date; or

upon the occurrence of specified corporate events described under Description of Notes Conversion Rights Conversion upon Specified Corporate Events.

On or after November 15, 2024 until the close of business on the business day immediately preceding February 15, 2025, holders may

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convert all or any portion of their notes, in multiples of $1,000 principal amount, at the option of the holder regardless of the foregoing circumstances.

The conversion rate for the notes is initially 236.7424 shares of common stock per $1,000 principal amount of notes (equivalent to an initial conversion price of approximately $4.22 per share of common stock), subject to adjustment as described in this prospectus supplement.

Upon conversion, we will pay or deliver, as the case may be, cash, shares of our common stock, or a combination of cash and shares of our common stock, at our election. If we satisfy our conversion obligation solely in cash or through payment and delivery, as the case may be, of a combination of cash and shares of our common stock, the amount of cash and shares of common stock, if any, due upon conversion will be based on a daily conversion value (as described herein) calculated on a proportionate basis for each trading day in a 25 trading-day observation period (as described herein). See Description of Notes Conversion Rights Settlement upon Conversion.

In addition, following certain corporate events that occur prior to the maturity date or if we deliver a notice of redemption, we will, in certain circumstances, increase the conversion rate for a holder who elects to convert its notes in connection with such a corporate event or notice of redemption, as the case may be, as described under Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption.

You will not receive any additional cash payment or additional shares representing accrued and unpaid interest, if any, upon conversion of a note, except in limited circumstances. Instead, interest will be deemed to be paid by the cash, shares of our common stock, or a combination of cash and shares of our common stock paid or delivered, as the case may be, to you upon conversion of a note.

Redemption at our Option

We may not redeem the notes prior to February 15, 2022. We may redeem for cash any or all of the notes, at our option, on or after February 15, 2022, if the last reported sale price of our common stock has been at least 130% of the conversion price for the notes then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding

the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date.

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No sinking fund is provided for the notes, which means that we are not required to redeem or retire the notes periodically.

We will give notice of any optional redemption not less than 30 scheduled trading days nor more than 60 calendar days before the redemption date by mail or electronic delivery to the trustee, the paying agent and each holder of notes. See Description of Notes Optional Redemption.

Fundamental Change

If we undergo a fundamental change (as defined under the heading Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes in this prospectus supplement) prior to the maturity date of the notes, subject to certain conditions, holders may require us to repurchase for cash all or part of their notes in principal amounts of $1,000 or a multiple thereof. The fundamental change repurchase price will be equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. See Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes.

Ranking

The notes will be our senior unsecured obligations and will rank:

- senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the notes;
- equal in right of payment to any of our unsecured indebtedness that is not so subordinated;
- effectively junior in right of payment to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and
- structurally junior to all existing and future indebtedness and other liabilities of our current or future subsidiaries (including trade payables).

As of September 30, 2018, we had $205.6 million of outstanding indebtedness for borrowed money (excluding intercompany debt). Our subsidiaries had $486.8 million of other liabilities including trade

payables but excluding intercompany obligations and liabilities of a type not required to be reflected on a balance sheet of such subsidiaries in accordance with U.S. generally accepted accounting principles (U.S. GAAP). After giving effect to the issuance of the notes (assuming no exercise of the underwriter s overallotment option to purchase additional notes, our and our subsidiaries indebtedness for borrowed money (excluding intercompany debt) would have been $405.6 million.

The indenture governing the notes does not limit the amount of debt that we or our current or future subsidiaries may incur.

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Certain Covenants	The indenture contains limitations on, among other things, our ability to consolidate, merge or dispose of all or substantially all of our assets. Although these types of transactions are permitted under the indenture, certain of the foregoing transactions could constitute a fundamental change permitting each holder to require us to repurchase the notes of such holder as described herein.
Use of Proceeds	We estimate that the net proceeds from this offering will be approximately $192.3 million (or approximately $221.3 million if the underwriter exercises its overallotment option to purchase additional notes in full), after deducting the underwriter s discount and estimated offering expenses payable by us. We intend to use the net proceeds we receive from sales of securities offered hereby to fund research and development to further develop and commercialize our portfolio of proprietary pharmaceutical and diagnostic products and for working capital, capital expenditures, acquisitions and other general corporate purposes, which will include the repayment or repurchase of indebtedness or debt securities outstanding from time to time including $28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit with an affiliate of our Chairman and Chief Executive Officer, Phillip Frost, M.D. See Use of Proceeds.
Book-Entry Form	The notes will be issued in book-entry form and will be represented by permanent global certificates deposited with, or on behalf of, The Depository Trust Company (DTC) and registered in the name of a nominee of DTC. Beneficial interests in any of the notes will be shown on, and transfers will be effected only through, records maintained by DTC or its nominee and any such interest may not be exchanged for certificated securities, except in limited circumstances.
Absence of a Public Market for the Notes	The notes are new securities and there is currently no established market for the notes. Accordingly, we cannot assure you as to the development or liquidity of any market for the notes. The underwriter has advised us that it currently intends to make a market in the notes. However, it is not obligated to do so, and it may discontinue any market making with respect to the notes without notice. We do not intend to apply for a listing of the notes on any securities exchange or any automated dealer quotation system.
U.S. Federal Income Tax Considerations	For certain U.S. federal income tax considerations applicable to the holding, disposition and conversion of the notes, and the holding and

	disposition of shares of our common stock, see U.S. Federal Income Tax Considerations.
Nasdaq Global Select Market Symbol for Our Common Stock	Our common stock is listed on the Nasdaq Global Select Market under the symbol OPK.
Trustee, Paying Agent and Conversion Agent	U.S. Bank National Association

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Governing Law	The notes and the indenture governing the notes will be governed by the laws of the State of New York.
Concurrent Offering of Borrowed Shares	Concurrently with this offering and by means of a separate prospectus supplement and accompanying prospectus, up to 30,000,000 of shares of our common stock will be offered by selling stockholders, who will borrow such shares through lending arrangements from an affiliate of the underwriter, which, as Share Borrower, is borrowing the shares from us. The borrowed shares are newly-issued shares issued in connection with this transaction and will be cancelled or held as treasury shares by us upon the expiration or the early termination of the share lending arrangements described herein. We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their investments in the notes. The selling stockholders may effect such transactions by selling the borrowed shares at various prices from time to time through the Share Borrower or its affiliates. The selling stockholders will receive all of the net proceeds from the sale of the borrowed shares, and we will not receive any of those proceeds, but we will receive from the Share Borrower a one-time nominal fee of $0.01 per share for each newly issued share. The concurrent offering of the borrowed shares is conditioned upon the closing of this offering. See Description of Share Lending Agreement and Underwriting.

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RISK FACTORS

An investment in the notes and in our common stock involves a high degree of risk. Before deciding whether to invest in the notes, you should carefully consider the risks described below, as well as the other risks and uncertainties described in our Annual Report on Form 10-K for the year ended December 31, 2017, the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed.

Risks Related to Our Business

We have a history of operating losses and may not become profitable in the near future.

We are not profitable and have incurred losses since our inception. We may not generate substantial revenue from the sale of proprietary pharmaceutical products or certain of our diagnostic products for some time and we have generated only limited revenue from our pharmaceutical operations in the U.S., Chile, Mexico, Israel, Spain and Ireland, and from sale of the *4Kscore* test. We may not successfully leverage the national marketing, sales and distribution resources of BioReference to enhance sales of, and reimbursement for, our *4Kscore* test and our other diagnostic products under development, which would adversely impact our ability to generate substantial revenue from the sale of these products for some time. *Rayaldee* is our only pharmaceutical product that has been approved for marketing, other than those products sold by our Chilean, Mexican, Israeli, Spanish and Irish subsidiaries. We continue to incur substantial research and development and general and administrative expenses related to our operations and, to date, we have devoted most of our financial resources to research and development, including our pre-clinical development activities and clinical trials. We may incur losses from our operations for the foreseeable future and these losses could increase as we continue our research activities and conduct development of, and seek regulatory approvals and clearances for, our product candidates, and prepare for and begin to commercialize any approved or cleared products, particularly if we are unable to generate profits and cash flow from BioReference and our other commercial businesses. If we are unable to generate profits and cash flow from BioReference and our other commercial businesses, our product candidates fail in clinical trials or do not gain regulatory approval or clearance, or if our approved products and product candidates do not achieve market acceptance, we may never become profitable. In particular, if we are unable to successfully commercialize *Rayaldee*, we may never generate substantial revenues from *Rayaldee* or achieve profitability. In addition, if we are required by the FDA to perform studies in addition to those we currently anticipate, our expenses will increase beyond current expectations and the timing of any potential product approval may be delayed. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

We will continue to require additional funding, which may not be available to us on acceptable terms, or at all.

As of September 30, 2018, we had cash and cash equivalents of approximately $43.7 million. We have not generated sustained positive cash flows sufficient to offset our operating and research and development expenses and our primary source of cash has been from the public and private placement of stock, the issuance of the 2033 Senior Notes and 2023 Convertible Notes (each as defined below) and credit facilities available to us.

On November 8, 2018, we entered into stock purchase agreements with certain investors pursuant to which we agreed to sell to such investors in private placements (the Private Placements) an aggregate of approximately 26.5 million shares of our common stock (the Shares) at a purchase price of $3.49 per share, which was the closing bid price of our common stock on the Nasdaq Global Select Market on such date, for an aggregate purchase price of $92.5 million. In addition, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to

provide us with an unsecured line of credit in the amount of $60 million. Borrowings under the line of credit will bear interest at a rate of 10% per annum and may be repaid and reborrowed at any time. The line of credit matures on November 8, 2023. On February 1, 2019, we borrowed $28.8 million under the line of credit; no amounts were previously outstanding under the line of credit. We intend

to use the proceeds of the $28.8 million borrowing to repurchase the 2033 Senior Notes (as defined below) tendered by holders thereof pursuant to such holders option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes. We intend to use a portion of the proceeds of this offering to repay the $28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit and to terminate the line of credit thereafter.

We believe that the cash and cash equivalents on hand or available to us from operations or through our lines of credit, together with the proceeds of this offering, are sufficient to meet our anticipated cash requirements for operations and debt service beyond the next 12 months. We have based this estimate on assumptions that may prove to be wrong or subject to change, and we may be required to use our available capital resources sooner than we currently expect or curtail aspects of our operations in order to preserve our capital.

Because of the numerous risks and uncertainties associated with the development and commercialization of our products and product candidates, the success of our relationships with Pfizer, VFMCRP and JT and the success of our integration of BioReference and other acquisitions, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials and our expanded commercial operations. Our future capital requirements will depend on a number of factors, including the successful commercialization of *Rayaldee*, our relationships with Pfizer, VFMCRP and JT, cash flow generated by BioReference and costs associated with the integration of the BioReference and other acquisitions, the continued progress of our research and development of product candidates, the timing and outcome of clinical trials and regulatory approvals, the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights, the status of competitive products, the availability of financing and our success in developing markets for our products and product candidates. Until we can generate a sufficient amount of product and service revenue to finance our cash requirements for research, development and operations, we will need to finance future cash needs primarily through public or private equity offerings, debt financings or strategic collaborations.

Our ability to obtain additional capital may depend on prevailing economic conditions and financial, business and other factors beyond our control. Disruptions in the U.S. and global financial markets may adversely impact the availability and cost of credit, as well as our ability to raise money in the capital markets. Economic conditions have been, and continue to be, volatile. Continued instability in these market conditions may limit our ability to replace, in a timely manner, maturing liabilities and access the capital necessary to fund and grow our business. Additionally, our continuing operating losses and the recent lawsuits involving us and our Chief Executive Officer (CEO) and Chairman of our Board of Directors (Chairman) by the SEC and other parties increase the difficulty in obtaining additional capital.

There can be no assurance that additional capital will be available to us on acceptable terms, or at all, which could adversely impact our business, results of operations, liquidity, capital resources and financial condition. If we are not able to secure additional funding when needed, we may have to delay reduce the scope of, or eliminate one or more of our clinical trials or research and development programs or cease operations altogether. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience additional significant dilution, and debt financing, if available, may involve restrictive covenants and other onerous terms. To the extent that we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or our products and product candidates or grant licenses on terms that may not be favorable to us.

Our research and development activities may not result in commercially viable products.

Many of our product candidates are in the early stages of development and are prone to the risks of failure inherent in drug, diagnostic and medical device product development. These risks further include the possibility that such

products would:

- be found to be ineffective, unreliable or otherwise inadequate or otherwise fail to receive regulatory approval;

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be difficult or impossible to manufacture on a commercial scale;

be uneconomical to market or otherwise not be effectively marketed;

fail to be successfully commercialized if adequate reimbursement from government health administration authorities, private health insurers and other organizations for the costs of these products is unavailable;

be impossible to commercialize because they infringe on the proprietary rights of others or compete with products marketed by others that are superior; or

fail to be commercialized prior to the successful marketing of similar products by competitors.

The results of pre-clinical trials and previous clinical trials for our products may not be predictive of future results, and our current and planned clinical trials may not satisfy the requirements of the FDA or other non-U.S. regulatory authorities.

Positive results from pre-clinical studies and early clinical trial experience should not be relied upon as evidence that later-stage or large-scale clinical trials will succeed. Likewise, there can be no assurance that the results of studies conducted by collaborators or other third parties will be viewed favorably or are indicative of our own future study results. We may be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are either (i) with respect to drugs or Class III devices, safe and effective for use in a diverse population of their intended uses or (ii) with respect to Class I or Class II devices, are substantially equivalent in terms of safety and effectiveness to devices that are already marketed under section 510(k) of the Food, Drug and Cosmetic Act. Success in early clinical trials does not mean that future clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and other non-U.S. regulatory authorities despite having progressed through initial clinical trials.

Further, our drug candidates may not be approved or cleared even if they achieve their primary endpoints in phase 3 clinical trials or registration trials. In addition, our diagnostic test candidates may not be approved or cleared, as the case may be, even though clinical or other data are, in our view, adequate to support an approval or clearance. The FDA or other non-regulatory authorities may disagree with our trial design and our interpretation of data from pre-clinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval or clearance of a product candidate even after reviewing and providing comment on a protocol for a pivotal clinical trial that has the potential to result in FDA and other non-U.S. regulatory authorities approval. Any of these regulatory authorities may also approve or clear a product candidate for fewer or more limited indications or uses than we request or may grant approval or clearance contingent on the performance of costly post-marketing clinical trials. The FDA or other non-U.S. regulatory authorities may not approve the labeling claims necessary or desirable for the successful commercialization of our product candidates.

The results of our clinical trials may show that our product candidates may cause undesirable side effects, which could interrupt, delay or halt clinical trials, resulting in the denial of regulatory approval by the FDA and other non-U.S. regulatory authorities.

Safety concerns with drug products over the years have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products, and establishment of risk management programs that may, for

instance, restrict distribution of drug products. Attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

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The failure to successfully commercialize Rayaldee would have a material adverse effect on our business.

In June 2016, the FDA approved our NDA for *Rayaldee* (calcifediol) extended release capsules for the treatment of SHPT in adults with stage 3 or 4 CKD and serum total 25-hydroxyvitamin D levels less than 30 ng/mL. The commercial launch for *Rayaldee* began in November 2016. *Rayaldee* is our only pharmaceutical product approved for marketing in the U.S. and our ability to generate revenue from product sales and achieve profitability is substantially dependent on our ability to effectively commercialize *Rayaldee*. Our failure to successfully commercialize *Rayaldee* would have a material adverse effect on our business, financial condition, cash flows and results of operations.

Additionally, the market perception and reputation of *Rayaldee* and its safety and efficacy are important to our business and the continued acceptance of our product candidates and products. Any negative publicity about *Rayaldee*, such as the discovery of safety issues, adverse events or even public rumors about such events, could have a material adverse effect on our business. Levels of market acceptance for *Rayaldee* could be impacted by several factors, some of which are not within our control, including but not limited to the:

- safety, efficacy, convenience and cost-effectiveness of our products compared to products of our competitors;
- scope of approved uses and marketing approval;
- availability of patent or regulatory exclusivity;
- timing of market approvals and market entry;
- ongoing regulatory obligations following approval;
- any restrictions or black box warnings required on the labeling of such products:
- availability of alternative products from our competitors;
- acceptance of the price of our products;
- effectiveness of our sales forces and promotional efforts;
- the level of reimbursement of our products;

acceptance of our products on government and private formularies;

ability to market our products effectively at the retail level or in the appropriate setting of care; and

the reputation of our products.

If *Rayaldee* fails to gain, or loses, market acceptance, our revenues would be adversely impacted and we may be required to take material impairment charges, all of which could have a material adverse effect on our business, financial condition, cash flows and results of operations.

We rely on licensing agreements with VFMCRP and JT for the international development and marketing of Rayaldee. Failure to maintain these license agreements could prevent us from successfully developing and commercializing Rayaldee worldwide.

In May 2016, EirGen, our wholly-owned subsidiary, partnered with VFMCRP through a Development and License Agreement (the VFMCRP Agreement) for the development and marketing of *Rayaldee* in Europe, Canada, Mexico, Australia, South Korea and certain other international markets. The license to VFMCRP potentially covers all therapeutic and prophylactic uses of the product in human patients, provided that initially the license is for the use of the product for the treatment or prevention of secondary hyperparathyroidism related to patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency. We received a non-refundable and non-creditable upfront payment of $50 million and a $2.0 million payment triggered by the approval of *Rayaldee* in Canada for the treatment of SHPT in adults with stage 3 or 4 CKD and vitamin D

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insufficiency. EirGen is also eligible to receive up to an additional $35 million in regulatory milestones and $195 million in launch and sales-based milestones. In addition, we are eligible to receive tiered, double digit royalty payments or a minimum royalty, whichever is greater, upon commencement of sales of the product. The success of the VFMCRP Agreement is dependent in part on, among other things, the skills, experience and efforts of VFMCRP s employees responsible for the project, VFMCRP s commitment to the arrangement and the financial condition of VFMCRP, all of which are beyond our control. In the event that VFMCRP, for any reason, including but not limited to early termination of the agreement, fails to devote sufficient resources to successfully develop and market *Rayaldee* internationally, our ability to earn milestone payments or receive royalty payments would be adversely affected, which would have a material adverse effect on our financial condition and prospects.

In October 2017, we entered into the JT Agreement under which JT was granted the exclusive rights for the development and commercialization of *Rayaldee* in Japan. The license grant to JT covers the therapeutic and preventative use of the product for (i) SHPT in non-dialysis and dialysis patients with CKD, (ii) rickets and (iii) osteomalacia, as well as such additional indications as may be added to the scope of the license subject to the terms of the JT Agreement. Under the terms of the JT Agreement, we received an initial upfront payment of $6 million and received another $6 million upon the initiation of our phase 2 study for *Rayaldee* in dialysis patients in the U.S. We are also eligible to receive up to an additional aggregate amount of $31 million upon the achievement of certain regulatory and development milestones by JT for *Rayaldee* in Japan, and $75 million upon the achievement of certain sales based milestones by JT. We will also receive tiered, double digit royalty payments at rates ranging from low double digits to mid-teens on net sales within Japan. JT will, at its sole cost and expense, be responsible for performing all development activities necessary to obtain all regulatory approvals for *Rayaldee* in Japan and for all commercial activities pertaining to *Rayaldee* in Japan, except for certain preclinical expenses for which we have agreed to reimburse JT up to a capped amount. If JT, for any reason, including but not limited to early termination of the JT Agreement, fails to devote sufficient resources to successfully develop and market *Rayaldee* in Japan, our ability to earn milestone payments or receive royalty payments would be adversely affected, which could have a material adverse effect on our financial condition and prospects.

Our exclusive worldwide agreement with Pfizer is important to our business. If we do not successfully develop hGH-CTP and/or Pfizer does not successfully commercialize hGH-CTP, our business could be adversely affected.

In December 2014, we entered into a development and commercialization agreement with Pfizer relating to our long-acting hGH-CTP for the treatment of Adult GHD and Pediatric GHD (the Pfizer Agreement). Under the terms of the Pfizer Agreement, we received non-refundable and non-creditable upfront payments of $295 million and are eligible to receive up to an additional $275 million upon the achievement of certain regulatory milestones. In addition, we are eligible to receive initial royalty payments associated with the commercialization of hGH-CTP for Adult GHD. Upon the launch of hGH-CTP for Pediatric GHD, the royalties will transition to a regional, tiered gross profit sharing for both hGH-CTP and Pfizer s Genotropin®. We are responsible for the development program and are obligated to pay for the development up to an agreed cap, which may be exceeded under certain circumstances. We will exceed the development cap and if we are unable to reach an agreement with Pfizer regarding cost sharing for the overruns as well as other obligations, including development obligations, it could have a material adverse impact on the expected benefits to us from the Pfizer transaction and our overall financial condition. In the event that the parties are able to obtain regulatory approvals to market a product covered by the Pfizer Agreement, we will be substantially dependent on Pfizer for the successful commercialization of such product. The success of the collaboration arrangement with Pfizer is dependent in part on, among other things, the skills, experience and efforts of Pfizer s employees responsible for the project, Pfizer s commitment to the arrangement, and the financial condition of Pfizer, all of which are beyond our control. In the event that Pfizer, for any reason, including but not limited to early termination of the Pfizer Agreement, fails to devote sufficient resources to successfully develop and commercialize any product resulting from the collaboration arrangement, our ability to earn milestone payments or receive royalty or profit

sharing payments would be adversely affected, which would have a material adverse effect on our financial condition and prospects and the trading prices of our securities.

Our business is substantially dependent on the success of clinical trials for hGH-CTP and our ability to achieve regulatory approval for the marketing of this product.

There is no assurance that clinical trials for hGH-CTP will be successful or support marketing approval, or that we will be able to obtain marketing approval for the product, or any other product candidate we are developing. Before they can be marketed, our products in development must be approved by the FDA or similar foreign governmental agencies. The process for obtaining FDA approval is both time-consuming and costly, with no certainty of a successful outcome. Before obtaining regulatory approval for the sale of any drug candidate, we must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Although the safety profile for hGH-CTP has been consistent with that observed with those treated with daily growth hormone, further testing or patient use may undermine those determinations or unexpected side effects may arise. A failure of any preclinical study or clinical trial can occur at any stage of testing. The results of preclinical and initial clinical testing of these products may not necessarily indicate the results that will be obtained from later or more extensive testing. It also is possible to suffer significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials. In December 2016, we announced preliminary topline data from our phase 3, double blind, placebo controlled study of hGH-CTP in adults with GHD. Although there was no statistically significant difference between hGH-CTP and placebo on the primary endpoint of change in trunk fat mass from baseline to 26 weeks, after unblinding the study, we identified an exceptional value of trunk fat mass reduction in the placebo group that may have affected the primary outcome. We completed post-hoc sensitivity analyses to evaluate the influence of outliers on the primary endpoint results using multiple statistical approaches. Analyses that excluded outliers showed a statistically significant difference between hGH-CTP and placebo on the change in trunk fat mass. Additional analyses that did not exclude outliers showed mixed results. There can be no assurance that a BLA will be submitted or that the FDA will consider the sensitivity analysis or consider the product for approval for adults with GHD. If phase 3 clinical trials for hGH-CTP are not successful or we are unable to achieve regulatory approval for this product, our business will be significantly adversely impacted, which could have a materially adverse effect on our business, financial condition and results of operations.

Our business is substantially dependent on our ability to develop, launch and generate revenue from our diagnostic products.

Our business is dependent on our ability to successfully commercialize the *4Kscore* test and other diagnostic products, including the *Claros 1*. We are committing significant resources to the development and commercialization of these products, and there is no guarantee that we will be able to successfully commercialize these tests. We have limited experience in developing, manufacturing, selling, marketing and distributing diagnostic tests. If we fail to leverage the national marketing, sales and distribution resources of BioReference to enhance sale of, and reimbursement for, the *4Kscore* test and other diagnostic products including the *Claros 1*, our ability to generate substantial revenue from the sale of these products will be adversely impacted. If we are not able to successfully develop, market or sell diagnostic tests we develop for any reason, including the failure to obtain any required regulatory approvals, obtain reimbursement for, or successfully integrate BioReference, we will not generate any meaningful revenue from the sale of such tests. Even if we are able to develop effective diagnostic tests for sale in the marketplace, a number of factors could impact our ability to sell such tests or generate any significant revenue from the sale of such tests, including without limitation:

our ability to establish and maintain adequate infrastructure to support the commercial launch and sale of our diagnostic tests, including establishing adequate laboratory space, information technology infrastructure, sample collection and tracking systems, electronic ordering and reporting systems and other infrastructure and hiring adequate laboratory and other personnel;

the success of the validation studies for our diagnostic tests under development and our ability to publish study results in peer-reviewed journals;

the availability of alternative and competing tests or products and technological innovations or other advances in medicine that cause our technologies to be less competitive;

the accuracy rates of such tests, including rates of false-negatives and/or false-positives;

concerns regarding the safety or effectiveness or clinical utility of our diagnostic tests;

changes in the regulatory environment affecting health care and health care providers, including changes in laws regulating laboratory testing and/or device manufacturers;

the extent and success of our sales and marketing efforts and ability to drive adoption of our diagnostic tests;

coverage and reimbursement levels by government payors and private insurers;

pricing pressures and changes in third-party payor reimbursement policies; and

intellectual property rights held by others or others infringing our intellectual property rights.

Our business is substantially dependent on our ability to generate profits and cash flow from our laboratory operations.

We have made a significant investment in our laboratory operations through the acquisition of BioReference. We compete in the clinical laboratory market primarily on the basis of the quality of testing, reporting and information systems, reputation in the medical community, the pricing of services and ability to employ qualified personnel. Our failure to successfully compete on any of these factors could result in the loss of clients and a reduction in our revenues and profits. To offset efforts by payors to reduce the cost and utilization of clinical laboratory services, we will need to obtain and retain new clients and business partners and grow the laboratory operations. A reduction in tests ordered, specimens submitted by existing clients or payment rates, without offsetting growth in our client base, could impact our ability to successfully grow our business and could have a material adverse impact on our ability to generate profits and cash flow from the laboratory operations.

Discontinuation or recalls of existing testing products, failure to develop, or acquire, licenses for new or improved testing technologies or our clients using new technologies to perform their own tests could adversely affect our business.

From time to time, manufacturers discontinue or recall reagents, test kits or instruments used by us to perform laboratory testing. Such discontinuations or recalls could adversely affect our costs, testing volume and revenue.

The clinical laboratory industry is subject to changing technology and new product introductions. Our success in maintaining a leadership position in genomic and other advanced testing technologies will depend, in part, on our ability to develop, acquire or license new and improved technologies on favorable terms and to obtain appropriate coverage and reimbursement for these technologies. We may not be able to negotiate acceptable licensing

arrangements and it cannot be certain that such arrangements will yield commercially successful diagnostic tests. If we are unable to license these testing methods at competitive rates, our research and development costs may increase as a result. In addition, if we are unable to license or develop new or improved technologies to expand our esoteric testing operations, our testing methods may become outdated when compared with our competition and testing volume and revenue may be materially and adversely affected.

Currently, most clinical laboratory testing is categorized as high or moderate complexity, and thereby is subject to extensive and costly regulation under Clinical Laboratory Improvement Amendments (CLIA). The cost of compliance with CLIA makes it impractical for most physicians to operate clinical laboratories in their offices, and other laws limit the ability of physicians to have ownership in a laboratory and to refer tests to such a laboratory. Manufacturers of laboratory equipment and test kits could seek to increase their sales by marketing

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point-of-care laboratory equipment to physicians and by selling test kits approved for home or physician office use to both physicians and patients. Diagnostic tests approved for home use are automatically deemed to be waived tests under CLIA and may be performed in physician office laboratories as well as by patients in their homes with minimal regulatory oversight. Other tests meeting certain FDA criteria also may be classified as waived for CLIA purposes. The FDA has regulatory responsibility over instruments, test kits, reagents and other devices used by clinical laboratories and has taken responsibility from the Centers for Disease Control for classifying the complexity of tests for CLIA purposes. Increased approval of waived test kits could lead to increased testing by physicians in their offices or by patients at home, which could affect our market for laboratory testing services and negatively impact our revenues. If our competitors develop and market products that are more effective, safer or less expensive than our products and product candidates, our net revenues, profitability and commercial opportunities will be negatively impacted.

If our competitors develop and market products or services that are more effective, safer or less expensive than our current and future products or services, our revenues, profitability and commercial opportunities will be negatively impacted.

The pharmaceutical, diagnostic and laboratory testing industries are highly competitive and require an ongoing, extensive search for technological innovation. The industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. They also require, among other things, the ability to effectively discover, develop, test and obtain regulatory approvals for products, as well as the ability to effectively commercialize, market and promote approved products.

Numerous companies, including major pharmaceutical companies, specialty pharmaceutical companies and specialized biotechnology companies, are engaged in the development, manufacture and marketing of pharmaceutical products competitive with those that we intend to commercialize ourselves and through our partners. Competitors to our diagnostics business include major diagnostic companies, reference laboratories, molecular diagnostic firms, universities and research institutions. Most of these companies have substantially greater financial and other resources, larger research and development staffs and more extensive marketing and manufacturing organizations than ours. This enables them, among other things, to make greater research and development investments and efficiently utilize their research and development costs, as well as their marketing and promotion costs, over a broader revenue base. This also provides our competitors with a competitive advantage in connection with the highly competitive product acquisition and product in-licensing process, which may include auctions in which the highest bidder wins. Our competitors may also have more experience and expertise in obtaining marketing approvals from the FDA and other regulatory authorities. We cannot predict with accuracy the timing or impact of the introduction of potentially competitive products or their possible effect on our sales. In addition to product development, testing, approval and promotion, other competitive factors in the pharmaceutical and diagnostics industry include industry consolidation, product quality and price, product technology, reputation, customer service and access to technical information.

In our clinical laboratory operations, we compete with three types of providers in a highly fragmented and competitive industry: hospital laboratories, physician-office laboratories and other independent clinical laboratories. Our major competitors in the New York metropolitan area are two of the largest national laboratories, Quest Diagnostics and Laboratory Corporation of America. We are much smaller than these national laboratories.

The clinical laboratory business is intensely competitive both in terms of price and service. Pricing of laboratory testing services is often one of the most significant factors used by health care providers and third-party payors in selecting a laboratory. As a result of the clinical laboratory industry undergoing significant consolidation, larger clinical laboratory providers are able to increase cost efficiencies afforded by large-scale automated testing. This consolidation results in greater price competition. We may be unable to increase cost efficiencies sufficiently, if at all,

and as a result, our net earnings and cash flows could be negatively impacted by such price competition. Additionally, we may also face changes in contracting with third-party payors, fee

schedules, competitive bidding for laboratory services or other actions or pressures reducing payment schedules as a result of increased or additional competition.

If our competitors market products that are more effective, safer, easier to use or less expensive than our current products and product candidates, or that reach the market sooner than our products and product candidates, we may not achieve commercial success. In addition, the biopharmaceutical, diagnostic, medical device and laboratory industries are characterized by rapid technological change. Because our research approach integrates many technologies, it may be difficult for us to stay abreast of the rapid changes in each technology. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies, products or product candidates obsolete or less competitive.

Our product development activities could be delayed or stopped.

We do not know whether our current or planned pre-clinical and clinical studies will be completed on schedule, or at all. Furthermore, we cannot guarantee that our planned pre-clinical and clinical studies will begin on time or at all. The commencement of our planned clinical trials could be substantially delayed or prevented by several factors, including:

- a limited number of, and competition for, suitable patients with the particular types of disease required for enrollment in our clinical trials or that otherwise meet the protocol s inclusion criteria and do not meet any of the exclusion criteria;
- a limited number of, and competition for, suitable serum or other samples from patients with particular types of disease required for our validation studies;
- a limited number of, and competition for, suitable sites to conduct our clinical trials;
- delay or failure to obtain FDA or other non-U.S. regulatory authorities approval or agreement to commence a clinical trial;
- delay or failure to obtain sufficient supplies of the product candidate for our clinical trials;
- requirements to provide the drugs, diagnostic tests or medical devices required in our clinical trial protocols or clinical trials at no cost or cost, which may require significant expenditures that we are unable or unwilling to make;
- delay or failure to reach agreement on acceptable clinical trial agreement terms or clinical trial protocols with prospective sites or investigators;

delay or failure to obtain institutional review board (IRB) approval to conduct or renew a clinical trial at a prospective site; and

insufficient liquidity to fund our preclinical and clinical studies.

The completion of our clinical trials could also be substantially delayed or prevented by several factors, including:

slower than expected rates of patient recruitment and enrollment;

failure of patients to complete the clinical trial;

unforeseen safety issues;

lack of efficacy evidenced during clinical trials;

termination of our clinical trials by one or more clinical trial sites;

inability or unwillingness of patients or medical investigators to follow our clinical trial protocols;

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inability to monitor patients adequately during or after treatment; and

insufficient liquidity to fund ongoing studies.

Our clinical trials may be suspended or terminated at any time by the FDA, other regulatory authorities, the IRB for any given site or us. Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. Amendments may require us to resubmit our clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial. Any failure or significant delay in commencing or completing clinical trials for our product candidates could materially harm our results of operations and financial condition, as well as the commercial prospects for our product candidates.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including in December 2018 and January 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

We currently have a seventy-nine person specialized sales and marketing team for Rayaldee in the U.S. If we are unable to develop or maintain a strong sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing Rayaldee or our other pharmaceutical products or product candidates in the U.S.

Other than our 79-person specialized sales and marketing team dedicated to *Rayaldee*, we currently have no pharmaceutical marketing, sales or distribution capabilities in the U.S. Any failure or inability to maintain adequate sales, marketing and distribution capabilities would adversely impact the commercialization of *Rayaldee* or our other pharmaceutical products or candidates. If we are not successful in commercializing our existing and future pharmaceutical products and product candidates, either on our own or through collaborations with one or more third parties, our product revenue will suffer and we may incur significant additional losses.

Our approved products or product candidates may have undesirable side effects and cause our products to be taken off the market.

If we or others identify undesirable side effects caused by our products:

regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;

regulatory authorities may withdraw their approval of the product and require us to take our approved product off the market;

we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;

we may have limitations on how we promote our products;

sales of products may decrease significantly;

we may be subject to litigation or product liability claims; and

our reputation may suffer.

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Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase our commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from its sale.

Our inability to meet regulatory quality standards applicable to our manufacturing and quality processes and to address quality control issues in a timely manner could delay the production and sale of our products or result in recalls of products.

Manufacturing or design defects, unanticipated use of our products or inadequate disclosure of risks relating to the use of our products could lead to injury or other adverse events. These events could lead to recalls or safety alerts relating to our products (either voluntary or required by governmental authorities) and could result, in certain cases, in the removal of a product from the market. Any recall could result in significant costs as well as negative publicity that could reduce demand for our products. Personal injuries relating to the use of our products can also result in product liability claims being brought against us. In some circumstances, such adverse events could also cause delays in new product approvals.

We are committed to providing high quality products to our customers, and we plan to meet this commitment by working diligently to continue implementing updated and improved quality systems and concepts throughout our organization. We cannot assure you that we will not have quality control issues in the future, which may result in warning letters and citations from the FDA. If we receive any warning letters from the FDA in the future, there can be no assurances regarding the length of time or cost it will take us to resolve such quality issues to our satisfaction and to the satisfaction of the FDA. If our remedial actions are not satisfactory to the FDA, we may have to devote additional financial and human resources to our efforts, and the FDA may take further regulatory actions against us including, but not limited to, assessing civil monetary penalties or imposing a consent decree on us, which could result in further regulatory constraints, including the governance of our quality system by a third party. Our inability to resolve these issues or the taking of further regulatory action by the FDA may weaken our competitive position and have a material adverse effect on our business, results of operations and financial condition.

We manufacture pharmaceutical products in Ireland, Mexico, Spain and Israel. We also prepare necessary test reagents and assemble and package the cassettes for our point-of-care diagnostic system at our facility in Woburn, Massachusetts. Any quality control issues at our facilities may weaken our competitive position and have a material adverse effect on our business results of operations and financial condition.

As a medical device manufacturer, we are required to register with the FDA and are subject to periodic inspection by the FDA for compliance with its Quality System Regulation (QSR) requirements, which require manufacturers of medical devices to adhere to certain regulations, including testing, quality control and documentation procedures. Compliance with applicable regulatory requirements is subject to continual review and is monitored rigorously through periodic inspections by the FDA. In addition, most international jurisdictions have adopted regulatory approval and periodic renewal requirements for medical devices, and we must comply with these requirements in order to market our products in these jurisdictions. In the European Community, we are required to maintain certain ISO certifications in order to sell our products and must undergo periodic inspections by notified bodies to obtain and maintain these certifications. Further, some emerging markets rely on the FDA s Certificate for Foreign Government (CFG) in lieu of their own regulatory approval requirements. Our failure, or our manufacturers failure to meet QSR, ISO or any other regulatory requirements or industry standards could delay production of our products and lead to fines, difficulties in obtaining regulatory clearances, recalls or other consequences, which could, in turn, have a material adverse effect on our business, results of operations and our financial condition.

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Failure to establish, and perform to, appropriate quality standards to assure that the highest level of quality is observed in the performance of our testing services could adversely affect the results of our operations and adversely impact our reputation.

The provision of clinical testing services, including anatomic pathology services and related services, and the design, manufacture and marketing of diagnostic products involve certain inherent risks. The services that we provide and the products that we design, manufacture and market are intended to provide information for healthcare providers in providing patient care. Therefore, users of our services and products may have a greater sensitivity to errors than the users of services or products that are intended for other purposes.

Similarly, negligence in performing our services can lead to injury or other adverse events. We may be sued under physician liability or other liability law for acts or omissions by our pathologists, laboratory personnel and other employees. We are subject to the attendant risk of substantial damages awards and risk to our reputation.

Even after we receive regulatory approval or clearance to market our product candidates, the market may not be receptive to our products.

Our products may not gain market acceptance among physicians, patients, health care payors and/or the medical community. We believe that the degree of market acceptance will depend on a number of factors, including:

timing of market introduction of competitive products;

safety and efficacy of our product compared to other products;

prevalence and severity of any side effects;

potential advantages or disadvantages over alternative treatments;

strength of marketing and distribution support;

price of our products, both in absolute terms and relative to alternative treatments;

availability of coverage and reimbursement from government and other third-party payors;

potential product liability claims;

limitations or warnings contained in a product s regulatory authority-approved labeling; and

changes in the standard of care for the targeted indications for any of our products or product candidates, which could reduce the marketing impact of any claims that we could make following applicable regulatory authority approval.

In addition, our efforts to educate the medical community and health care payors on the benefits of our products and product candidates may require significant resources and may never be successful. If our products do not gain market acceptance, it would have a material adverse effect on our business, results of operations and financial condition.

If our products are not covered and eligible for reimbursement from government and third-party payors, we may not be able to generate significant revenue or achieve or sustain profitability.

The coverage and reimbursement status of newly approved or cleared drugs, diagnostic and laboratory tests is uncertain, and failure of our pharmaceutical products, diagnostic tests or laboratory tests to be adequately covered by insurance and eligible for adequate reimbursement could limit our ability to market any future product candidates we may develop and decrease our ability to generate revenue from any of our existing and future product candidates that may be approved or cleared. The commercial success of our existing and future products in both domestic and international markets will depend in part on the availability of coverage and

adequate reimbursement from third-party payors, including government payors, such as the Medicare and Medicaid programs, managed care organizations and other third-party payors, as well as our ability to obtain in network status with such payors. The government and other third-party payors are increasingly attempting to contain health care costs by limiting both insurance coverage and the level of reimbursement for new drugs and diagnostic tests and restricting in-network status of laboratory providers. As a result, they may not cover or provide adequate payment for our product candidates. These payors may conclude that our products are less safe, less effective or less cost-effective than existing or later-introduced products. These payors may also conclude that the overall cost of the procedure using one of our devices exceeds the overall cost of the competing procedure using another type of device, and third-party payors may not approve our products for insurance coverage and adequate reimbursement or approve our laboratory for in network status.

The failure to obtain coverage and adequate or any reimbursement for our products, or health care cost containment initiatives that limit or restrict reimbursement for our products, may reduce any future product revenue. Even though a drug (not administered by a physician) may be approved by the FDA, this does not mean that a Prescription Drug Plan (PDP), a private insurer operating under Medicare Part D, will list that drug on its formulary or will set a reimbursement level. PDPs are not required to make every FDA-approved drug available on their formularies. If our drug products are not listed on sufficient number of PDP formularies or if the PDPs levels of reimbursement are inadequate, our business, results of operations and financial condition could be materially adversely affected. Private health plans, such as managed care plans and pharmacy benefit management (PBM) programs may also not include our products on formularies, use other techniques that may restrict access to our products or set a lower reimbursement rate than anticipated.

On May 18, 2018, Novitas, the MAC for a jurisdiction that includes the State of New Jersey, where our 4*KScore* test samples are processed, issued a draft non-coverage determination (LCD) that proposed no coverage for our 4*KScore* test. We submitted comments to the draft LCD during the public comment period, which ended on July 5, 2018. In January 2019, Notivas issued a notice of future non-coverage determination for the 4*KScore* test to be effective March 20, 2019. We are currently evaluating options to appeal the decision and undertake other steps with CMS in an effort to have this determination rescinded or reversed, however, there can be no assurance that we will be successful in doing so. If we are not able to successfully appeal Novitas decision, we may not be able to obtain Medicare reimbursement for the 4*KScore* test, which could result in a loss of revenues and could have a material adverse effect on our cash flows, results of operations, net income, financial conditions and the trading prices of our securities.

A significant portion of our revenues come from government subsidized healthcare programs such as Medicaid and Medicare. Our failure to comply with applicable Medicare, Medicaid and other governmental payor rules could result in our inability to participate in a governmental payor program, our returning funds already paid to us, civil monetary penalties, criminal penalties and/or limitations on the operational function of our laboratory. If we were unable to receive reimbursement under a governmental payor program, a substantial portion of our revenues would be lost, which would adversely affect our results of operations and financial condition. In addition, if a federal government shutdown were to occur for a prolonged period of time, federal government payment obligations, including its obligations under Medicaid and Medicare, may be delayed. Similarly, if state government shutdowns were to occur, state payment obligations may be delayed. If the federal or state governments fail to make payments under these programs on a timely basis, our business could suffer, and our financial position, results of operations or cash flows may be materially affected.

As we evolve from a company primarily involved in development to a company also involved in commercialization of our pharmaceutical and diagnostic products as well as our laboratory testing services, we may encounter difficulties in managing our growth and expanding our operations successfully.

As we advance our product candidates and expand our business, we will need to expand our development, regulatory and commercial infrastructure. As our operations expand, we expect that we will need to manage additional relationships with various third parties, collaborators and suppliers. Maintaining these relationships and managing our future growth will impose significant added responsibilities on members of our management. We must be able to: manage our development efforts and operations effectively; manage our clinical trials

effectively; hire, train and integrate additional management, administrative and sales and marketing personnel; improve our managerial, development, operational and finance systems; implement and manage an effective marketing strategy; and expand our facilities, all of which may impose a strain on our administrative and operational infrastructure.

Furthermore, we may acquire additional businesses, products or product candidates that complement or augment our existing business. Integrating any newly acquired business or product could be expensive and time-consuming. We may not be able to integrate any acquired business or product successfully or operate any acquired business profitably. Our future financial performance will depend, in part, on our ability to manage any future growth effectively and our ability to integrate any acquired businesses. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company, which would have a material adverse effect on our business, results of operations and financial condition.

Our success is dependent to a significant degree upon the involvement, efforts and reputation of our Chairman and Chief Executive Officer, Phillip Frost, M.D.

Our success is dependent to a significant degree upon the efforts of our Chairman and CEO, Phillip Frost, M.D., who is essential to our business. The departure of our CEO for whatever reason or the inability of our CEO to continue to serve in his present capacity could have a material adverse effect upon our business, financial condition and results of operations. Our CEO has a highly regarded reputation in the pharmaceutical and medical industry and attracts business opportunities and assists both in negotiations with acquisition targets, investment targets and potential joint venture partners. Our CEO has also provided financing to us, both in terms of a credit agreement and equity investments. If we lost his services or if his reputation was damaged for whatever reason, including, but not limited to, as a result of the allegations underlying various SEC and shareholder lawsuits against us and Dr. Frost, our relationships with acquisition and investment targets, joint ventures, customers and investors, as well as our ability to obtain additional funding on acceptable terms, or at all, may suffer and could cause a material adverse impact on our operations, financial condition and the value of our common stock.

If we fail to attract and retain key management and scientific personnel, we may be unable to successfully operate our business and develop or commercialize our products and product candidates.

We will need to expand and effectively manage our managerial, operational, sales, financial, development and other resources in order to successfully operate our business and pursue our research, development and commercialization efforts for our products and product candidates. Our success depends on our continued ability to attract, retain and motivate highly qualified management and pre-clinical and clinical personnel. The loss of the services or support of any of our senior management, particularly Dr. Phillip Frost, our Chairman and CEO, could delay or prevent the development and commercialization of our products and product candidates.

If the FDA or other applicable regulatory authorities approve generic products that compete with any of our products or product candidates, the sale of our products or product candidates may be adversely affected.

Once an NDA is approved, the product covered thereby becomes a listed drug which, in turn can be relied upon by potential competitors in support of an approval of an abbreviated new drug application (ANDA) or 505(b)(2) application. U.S. laws and other applicable policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for a generic substitute. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use, or labeling, as our product or product candidate and that the generic product is bioequivalent to ours, meaning it is absorbed in the body

at the same rate and to the same extent as our product or product candidate. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a

significant percentage of sales of any branded product is typically lost to the generic product. Accordingly, competition from generic equivalents to our products or product candidates would materially adversely impact our revenues, profitability and cash flows and substantially limit our ability to obtain a return on the investments that we have made in our products and product candidates.

In 2017, Congress reauthorized the Generic Drug User Fee Act (the GDUFA). The generic drug user fee program, established in 2012, is designed to speed the approval of new generic drugs. In addition, over the past few months, the FDA has used its regulatory authority to enact other programs to streamline the path to market for generic drugs. In addition, a regulatory pathway for biosimilars was established in 2012 including a new user fee program to promote the development of these products that show no clinically meaningful differences from innovator biologics. Though they have their own statutory market pathway, like generic drugs, biosimilars can receive FDA approval by providing less clinical data than the innovator product. Biosimilars are expected to be less expensive competitors to innovator biologics reducing prices overall. We anticipate several new biosimilars reaching the market over the next year.

If we fail to acquire and develop other products or product candidates at all or on commercially reasonable terms, we may be unable to diversify or grow our business.

We intend to continue to rely on acquisitions and in-licensing as a source of our products and product candidates for development and commercialization. The success of this strategy depends upon our ability to identify, select and acquire pharmaceutical and diagnostic products, drug delivery technologies and medical device product candidates. Proposing, negotiating and implementing an economically viable product acquisition or license is a lengthy and complex process. We compete for partnering arrangements and license agreements with pharmaceutical, biotechnology and medical device companies and academic research institutions. Our competitors may have stronger relationships with third parties with whom we are interested in collaborating and/or may have more established histories of developing and commercializing products.

Most of our competitors also have substantially greater financial and other resources than us. As a result, our competitors may have a competitive advantage in entering into partnering arrangements with such third parties, as such partnering arrangements are often decided in an auction process in which the highest bidder wins. In addition, even if we find promising products and product candidates, and generate interest in a partnering or strategic arrangement to acquire such products or product candidates, we may not be able to acquire rights to additional product candidates or approved products on terms that we find acceptable, or at all.

We expect that any product candidate to which we acquire rights will require additional development efforts prior to commercial sale, including extensive clinical testing and approval or clearance by the FDA and other non-U.S. regulatory authorities. All product candidates are subject to the risks of failure inherent in pharmaceutical, diagnostic test or medical device product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. Even if the product candidates are approved or cleared for marketing, we cannot be sure that they would be capable of economically feasible production or commercial success. If we fail to acquire or develop other product candidates that are capable of economically feasible production and commercial success, our business, results of operations and financial condition and cash flows may be materially adversely affected.

We rely on third parties to manufacture and supply our pharmaceutical and diagnostic products and product candidates.

If our manufacturing partners are unable to produce our products in the amounts that we require, we may not be able to establish a contract and obtain a sufficient alternative supply from another supplier on a timely basis and in the

quantities we require. We expect to continue to depend on third-party contract manufacturers for the foreseeable future.

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Our products and product candidates require precise, high quality manufacturing. Any of our contract manufacturers will be subject to ongoing periodic unannounced inspection by the FDA and other non-U.S. regulatory authorities to ensure strict compliance with QSR regulations for devices or current Good Manufacturing Practices (cGMPs) for drugs, and other applicable government regulations and corresponding standards relating to matters such as testing, quality control and documentation procedures. If our contract manufacturers fail to achieve and maintain high manufacturing standards in compliance with QSR or cGMPs, we may experience manufacturing errors resulting in patient injury or death, product recalls or withdrawals, delays or interruptions of production or failures in product testing or delivery, delay or prevention of filing or approval of marketing applications for our products, cost overruns or other problems that could seriously harm our business.

Any performance failure on the part of our contract manufacturers could delay clinical development or regulatory approval or clearance of our product candidates or commercialization of our products and product candidates, depriving us of potential product revenue and resulting in additional losses. In addition, our dependence on a third party for manufacturing may adversely affect our future profit margins. Our ability to replace an existing manufacturer may be difficult because the number of potential manufacturers is limited and the FDA must approve any replacement manufacturer before it can begin manufacturing our products or product candidates. Such approval would result in additional non-clinical testing and compliance inspections. It may be difficult or impossible for us to identify and engage a replacement manufacturer on acceptable terms in a timely manner, or at all.

Independent clinical investigators and contract research organizations that we engage to conduct our clinical trials may not be diligent, careful or timely.

We depend on independent clinical investigators to conduct our clinical trials. Contract research organizations may also assist us in the collection and analysis of data. These investigators and contract research organizations will not be our employees, and we will not be able to control, other than by contract, the amount of resources, including time, that they devote to products that we develop. If independent investigators fail to devote sufficient resources to the development of product candidates or clinical trials, or if their performance is substandard, it will delay the marketing approval or clearance and commercialization of any products that we develop. Further, the FDA requires that we comply with standards, commonly referred to as good clinical practice, for conducting, recording and reporting clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial subjects are protected. If our independent clinical investigators and contract research organizations fail to comply with good clinical practice, the results of our clinical trials could be called into question and the clinical development of our product candidates could be delayed.

Failure of clinical investigators or contract research organizations to meet their obligations to us or comply with federal regulations and good clinical practice procedures could adversely affect the clinical development of our product candidates and harm our business, results of operations and financial condition.

If the validity of an informed consent from a subject was to be challenged, it may negatively impact our product development efforts.

We take steps to ensure that all clinical data and genetic and other biological samples are collected from subjects who provide informed consent for the data and samples as required by applicable laws and we work to ensure that the subjects from whom our data and samples are collected do not retain any proprietary or commercial rights to the data or samples or any discoveries derived from them. However, because we may collect data and samples from countries that are governed by a number of different regulatory regimes, there are many complex legal questions relating to the adequacy of informed consent that we must continually address. The adequacy of any given subject s informed consent may be challenged in the future, and any given informed consent may prove unlawful or otherwise inadequate for our

purposes. Any findings against us, or our clinical

collaborators, could obligate us to stop using some of our clinical samples, which in turn may hinder our product development efforts. Such a result would also likely involve legal challenges that may consume our management and financial resources.

Failure to timely or accurately bill and collect for our services could have a material adverse effect on our revenues and our business.

Billing for laboratory testing services is extremely complicated and is subject to extensive and non-uniform rules and administrative requirements. Depending on the billing arrangement and applicable law, we bill various payors, such as patients, insurance companies, Medicare, Medicaid, physicians, hospitals and employer groups. Changes in laws and regulations and payor practices increase the complexity and cost of our billing process. Additionally, in the U.S., third-party payors generally require billing codes on claims for reimbursement that describe the services provided. For laboratory services, the American Medical Association establishes most of the billing codes using a data code set called Current Procedural Terminology (CPT) codes and the World Health Organization establishes diagnostic codes using a data set called International Statistical Classification of Diseases (ICD-10) codes. Each third-party payor generally develops payment amounts and coverage policies for their beneficiaries or members that ties to the CPT code established for the laboratory test and the ICD-10 code selected by the ordering or performing physician. Therefore, coverage and reimbursement may differ by payor even if the same billing code is reported for claims filing purposes. For laboratory tests without a specific billing code, payors often review claims on a claim-by-claim basis and there are increased uncertainties as to coverage and eligibility for reimbursement.

In addition to the items described above, third-party payors, including government programs, may decide to deny payment or recoup payments for testing that they contend was improperly billed or not medically necessary, against their coverage determinations, or for which they believe they have otherwise overpaid (including as a result of their own error), and we may be required to refund payments already received. Our revenues may be subject to retroactive adjustment as a result of these factors among others, including without limitation, differing interpretations of billing and coding guidance and changes by government agencies and payors in interpretations, requirements and conditions of participation in various programs.

We implemented a new billing system for our laboratory business in the third quarter of 2016. The adoption of the new billing system, which replaced the old billing system, poses several challenges relating to, among other things, training of personnel, communication of new rules and procedures, changes in corporate culture, migration of data and the potential instability of the new system. As an integral part of our billing compliance program, we assess our billing and coding practices in the ordinary course of business, respond to payor audits on a routine basis and investigate reported failures or suspected failures to comply with federal and state healthcare reimbursement requirements as well as overpayment claims which may arise from time to time without fault on the part of us. We have in the ordinary course of business been the subject of recoupments by payors and have from time to time identified and reimbursed payors for overpayments.

Incorrect or incomplete documentation and billing information, as well as the other items described above, among other factors, could result in non-payment for services rendered or having to pay back amounts incorrectly billed and collected. Further, the failure to timely or correctly bill could lead to various penalties, including: (1) exclusion from participation in the CMS and other government programs; (2) asset forfeitures; (3) civil and criminal fines and penalties; and (4) the loss of various licenses, certificates and authorizations necessary to operate our business, any of which could have a material adverse effect on our results of operations or cash flows.

Failure in our information technology systems, including by cybersecurity attacks or other data security incidents, could significantly increase testing turn-around time or billing processes and otherwise disrupt our operations.

Our operations depend, in part, on the continued performance of our information technology systems. Our information technology systems are potentially vulnerable to physical or electronic break-ins, computer viruses

and similar disruptions. In addition, we are in the process of integrating the information technology systems of our subsidiaries, and we may experience system failures or interruptions as a result of this process. Sustained system failures or interruption of our systems in one or more of our laboratory operations could disrupt our ability to process laboratory requisitions, perform testing, provide test results in a timely manner and/or bill the appropriate party. Failure of our information technology systems could adversely affect our business, profitability and financial condition.

A successful cybersecurity attack or other data security incident could result in the misappropriation and/or loss of confidential or personal information, create system interruptions, or deploy malicious software that attacks our systems. It is possible that a cybersecurity attack might not be noticed for some period of time. The occurrence of a cybersecurity attack or incident could result in business interruptions from the disruption of our information technology systems, or negative publicity resulting in reputational damage with our customers, shareholders and other stakeholders and/or increased costs to prevent, respond to or mitigate cybersecurity events. In addition, the unauthorized dissemination of sensitive personal information or proprietary or confidential information could expose us or other third parties to regulatory fines or penalties, litigation and potential liability, or otherwise harm our business.

Healthcare plans have taken steps to control the utilization and reimbursement of healthcare services, including clinical test services.

We also face efforts by non-governmental third-party payors, including healthcare plans, to reduce utilization and reimbursement for clinical testing services.

The healthcare industry has experienced a trend of consolidation among healthcare insurance plans, resulting in fewer but larger insurance plans with significant bargaining power to negotiate fee arrangements with healthcare providers, including clinical testing providers. These healthcare plans, and independent physician associations, may demand that clinical testing providers accept discounted fee structures or assume all or a portion of the financial risk associated with providing testing services to their members through capped payment arrangements. In addition, some healthcare plans limit the laboratory network to only a single national or regional laboratory to obtain improved fee-for-service pricing. There is also an increasing number of patients enrolling in consumer driven products and high deductible plans that involve greater patient cost-sharing.

The increased consolidation among healthcare plans also has increased the potential adverse impact of ceasing to be a contracted provider with any such insurer.

We expect continuing efforts to limit the number of participating laboratories in payor networks, reduce reimbursements, impose more stringent cost controls and reduce utilization of clinical test services. These efforts, including future changes in third-party payor rules, practices and policies, or failing to become a contracted provider or ceasing to be a contracted provider to a healthcare plan, may have a material adverse effect on our business.

The success of our business may be dependent on the actions of our collaborative partners.

We have entered into and expect in the future to enter into collaborative arrangements with established multi-national pharmaceutical, diagnostic and medical device companies, which will finance or otherwise assist in the development, manufacture and marketing of products incorporating our technology. We anticipate deriving some revenues from research and development fees, license fees, milestone payments and royalties from collaborative partners. Our prospects, therefore, may depend to some extent upon our ability to attract and retain collaborative partners and to develop technologies and products that meet the requirements of prospective collaborative partners. In addition, our

collaborative partners may have the right to abandon research projects, guide strategy regarding prosecution of relevant patent applications and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed-upon research terms. There can be no

assurance that we will be successful in establishing collaborative arrangements on acceptable terms or at all, that collaborative partners will not terminate funding before completion of projects, that our collaborative arrangements will result in successful product commercialization or that we will derive any revenues from such arrangements. To the extent that we are unable to develop and maintain collaborative arrangements, we would need substantial additional capital to undertake research, development and commercialization activities on our own.

If we are unable to obtain and enforce patent protection for our products, our business could be materially harmed.

Our success depends, in part, on our ability to protect proprietary methods and technologies that we develop or license under the patent and other intellectual property laws of the U.S. and other countries, so that we can prevent others from unlawfully using our inventions and proprietary information. However, we may not hold proprietary rights to some patents required for us to commercialize our products and product candidates. Because certain U.S. patent applications are confidential, third parties may have filed patent applications for technology covered by our pending patent applications without our being aware of those applications, and our patent applications may not have priority over those applications. For this and other reasons, we or our third-party collaborators may be unable to secure desired patent rights, thereby losing desired exclusivity. If licenses are not available to us on acceptable terms, we may not be able to market the affected products or conduct the desired activities, unless we challenge the validity, enforceability or infringement of the third-party patent or otherwise circumvent the third-party patent.

Our strategy depends on our ability to rapidly identify and seek patent protection for our discoveries. In addition, we will rely on third-party collaborators to file patent applications relating to proprietary technology that we develop jointly during certain collaborations. The process of obtaining patent protection is expensive and time-consuming. If our present or future collaborators fail to file and prosecute all necessary and desirable patent applications at a reasonable cost and in a timely manner, our business will be adversely affected. Unauthorized parties may be able to obtain and use information that we regard as proprietary.

The issuance of a patent does not guarantee that it is valid or enforceable. Any patents we have obtained, or obtain in the future, may be challenged, invalidated, unenforceable or circumvented. Moreover, the U.S. Patent and Trademark Office (the USPTO) may commence interference proceedings involving our patents or patent applications. In addition, court decisions may introduce uncertainty in the enforceability or scope of patents owned by biotechnology, pharmaceutical and medical device companies. Any challenge to, finding of unenforceability or invalidation or circumvention of, our patents or patent applications would be costly, would require significant time and attention of our management, and could have a material adverse effect on our business, results of operations and financial condition.

Our pending patent applications may not result in issued patents. The patent position of pharmaceutical, biotechnology, diagnostic and medical device companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards that the USPTO and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in pharmaceutical, biotechnology, diagnostic or medical device patents. Accordingly, we do not know the degree of future protection for our proprietary rights or the breadth of claims that will be allowed in any patents issued to us or to others. The legal systems of certain countries do not favor the aggressive enforcement of patents, and the laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. Therefore, the enforceability or scope of our owned or licensed patents in the U.S. or in foreign countries cannot be predicted with certainty, and, as a result, any patents that we own or license may not provide sufficient protection against competitors. We may not be able to obtain or maintain patent protection for our pending patent applications, those we may file in the future or those we may license from third parties.

We cannot assure you that any patents that have issued, that may issue, or that may be licensed to us will be enforceable or valid, or will not expire prior to the commercialization of our products and product candidates,

thus allowing others to more effectively compete with us. Therefore, any patents that we own or license may not adequately protect our products and product candidates or our future products, which could have a material adverse effect on our business, results of operations and financial condition.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.

In addition to patent protection, we also rely on other proprietary rights, including protection of trade secrets, know-how and confidential and proprietary information. To maintain the confidentiality of trade secrets and proprietary information, we will seek to enter into confidentiality agreements with our employees, consultants and collaborators upon the commencement of their relationships with us. These agreements generally require that all confidential information developed by the individual or made known to the individual by us during the course of the individual s relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees also generally provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property.

However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our confidential information. The disclosure of our trade secrets would impair our competitive position and may materially harm our business, financial condition and results of operations.

We will rely heavily on licenses from third parties. Failure to comply with the provisions of these licenses could result in the loss of our rights under the license agreements.

Many of the patents and patent applications in our patent portfolio are not owned by us, but are licensed from third parties. Such license agreements give us rights for the commercial exploitation of the patents resulting from the respective patent applications, subject to certain provisions of the license agreements. Failure to comply with these provisions could result in the loss of our rights under these license agreements. Our inability to rely on these patents and patent applications, which are the basis of our technology, would have a material adverse effect on our business, results of operations and financial condition.

We license patent rights to certain of our technology from third-party owners. If such owners do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects will be harmed.

We have obtained licenses from, among others, INEOS Healthcare, the President and Fellows of Harvard College, The Scripps Research Institute, Arctic Partners, TESARO and Academia Sinica, that are necessary or useful for our business. In addition, we intend to enter into additional licenses of third-party intellectual property in the future. We cannot guarantee that no third parties will step forward and assert inventorship or ownership in our in-licensed patents. In some cases, we may rely on the assurances of our licensors that all ownership rights have been secured and that all necessary agreements are intact or forthcoming.

Our success will depend in part on our ability or the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property and, in particular, those patents to which we have secured exclusive rights in our field. We or our licensors may not successfully prosecute the patent applications which are licensed to us. Even if patents issue in respect of these patent applications, we or our licensors may fail to maintain these patents or may determine not to pursue litigation against other companies that are infringing these

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patents. Without protection for the intellectual property we have licensed, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business, results of operations and financial condition.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties.

Other entities may have or obtain patents or proprietary rights that could limit our ability to develop, manufacture, use, sell, offer for sale or import products or impair our competitive position. In addition, other entities may have or obtain patents or proprietary rights that cover our current research and preclinical studies. The U.S. case law pertaining to statutory exemptions to patent infringement for those who are using third-party patented technology in the process of pursuing FDA regulatory approval changes over time. Lawsuits involving such exemptions are very fact intensive and it is currently unclear under U.S. case law whether preclinical studies would always qualify for such an exemption, and whether such exemptions would apply to research tools. To the extent that our current research and preclinical studies may be covered by the patent rights of others, the risk of suit may continue after such patents expire because the statute of limitations for patent infringement runs for six years. To the extent that a third party develops and patents technology that covers our products, we may be required to obtain licenses to that technology, which licenses may not be available or may not be available on commercially reasonable terms, if at all. If licenses are not available to us on acceptable terms, we will not be able to market the affected products or conduct the desired activities, unless we challenge the validity, enforceability or infringement of the third-party patent, or circumvent the third-party patent, which would be costly and would require significant time and attention of our management. Third parties may have or obtain by license or assignment valid and enforceable patents or proprietary rights that could block us from developing products using our technology. Our failure to obtain a license to any technology that we require may materially harm our business, financial condition and results of operations.

If we become involved in patent litigation or other proceedings related to a determination of rights, we could incur substantial costs and expenses, substantial liability for damages or be required to stop our product development and commercialization efforts.

Third parties may sue us for infringing their patent rights. Likewise, we may need to resort to litigation to enforce a patent issued or licensed to us or to determine the scope and validity of proprietary rights of others. In addition, a third party may claim that we have improperly obtained or used its confidential or proprietary information. Furthermore, in connection with our third-party license agreements, we generally have agreed to indemnify the licensor for costs incurred in connection with litigation relating to intellectual property rights. The cost to us of any litigation or other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial, and the litigation would divert our management s efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations. Our involvement in patent litigation and other proceedings could have a material adverse effect on our business, results of operations and financial condition.

If any parties successfully claim that our creation or use of proprietary technologies infringes upon their intellectual property rights, we might be forced to pay damages, potentially including treble damages, if we are found to have willfully infringed on such parties patent rights. In addition to any damages we might have to pay, a court could require us to stop the infringing activity or obtain a license. Any license required under any patent may not be made available on commercially acceptable terms, if at all. In addition, such licenses are likely to be non-exclusive and, therefore, our competitors may have access to the same technology licensed to us. If we fail to obtain a required license and are unable to design around a patent, we may be unable to effectively market some of our technology and

products, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations.

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We have faced, and may in the future face, intellectual property infringement claims that could be time-consuming and costly to defend, and could result in our loss of significant rights and the assessment of treble damages.

We may from time to time receive notices of claims of infringement and misappropriation or misuse of other parties proprietary rights. Some of these additional claims may also lead to litigation. We cannot assure you that we will prevail in such actions, or that other actions alleging misappropriation or misuse by us of third-party trade secrets, infringement by us of third-party patents and trademarks or the validity of our patents, will not be asserted or prosecuted against us.

We may also initiate claims to defend our intellectual property or to seek relief on allegations that we use, sell or offer to sell technology that incorporates third-party intellectual property. Intellectual property litigation, regardless of outcome, is expensive and time-consuming, could divert management s attention from our business and have a material negative effect on our business, operating results or financial condition. If there is a successful claim of infringement against us, we may be required to pay substantial damages (including treble damages if we were to be found to have willfully infringed a third party s patent) to the party claiming infringement, develop non-infringing technology, stop selling our tests or using technology that contains the allegedly infringing intellectual property or enter into royalty or license agreements that may not be available on acceptable or commercially practical terms, if at all. Our failure to develop non-infringing technologies or license the proprietary rights on a timely basis could harm our business.

It is possible that a third party or patent office might take the position that one or more patents or patent applications constitute prior art in the field of genomic-based diagnostics. In such a case, we might be required to pay royalties, damages and costs to firms who own the rights to these patents, or we might be restricted from using any of the inventions claimed in those patents.

We may become subject to product liability for our diagnostic tests, clinical trials, pharmaceutical products and medical device products.

Our success depends on the market s confidence that we can provide reliable, high-quality pharmaceuticals, medical devices and diagnostics tests. Our reputation and the public image of our products or technologies may be impaired if our products fail to perform as expected or our products are perceived as difficult to use. Our products are complex and may develop or contain undetected defects or errors. Furthermore, if a product or a future product candidate harms people, or is alleged to be harmful, we may be subject to costly and damaging product liability claims brought against us by clinical trial participants, consumers, health care providers, corporate partners or others. We have product liability insurance covering commercial sales of current products and our ongoing clinical trials. Any defects or errors could lead to the filing of product liability claims, which could be costly and time-consuming to defend and result in substantial damages. If we experience a sustained material defect or error, this could result in loss or delay of revenues, delayed market acceptance, damaged reputation, diversion of development resources, legal claims, increased insurance costs or increased service and warranty costs, any of which could materially harm our business. We cannot assure you that our product liability insurance would protect our assets from the financial impact of defending a product liability claim. A product liability claim could have a serious adverse effect on our business, financial condition and results of operations.

We are the subject of pending civil litigation which could require us to pay substantial damages or could otherwise have a material adverse effect on us.

On September 7, 2018, the SEC filed a lawsuit in the Southern District of New York (the Complaint), against a number of individuals and entities (each a Defendant and, collectively, the Defendants) including us and our CEO and

Chairman, Dr. Phillip Frost. The SEC alleged that we (i) aided and abetted a purported pump and dump scheme in connection with one company perpetrated by a number of the Defendants, and (ii) failed to file required Schedules 13D or 13G with the SEC. The Complaint also alleged that Dr. Frost

(i) participated in the alleged market manipulation in connection with two companies, (ii) failed to file required Schedule 13Ds with the SEC, and (iii) sold unregistered securities without an applicable exemption. Following the SEC s announcement of the Complaint, a number of class action and derivative suits were filed against us and our directors and officers concerning the allegations in the Complaint and related matters.

In December 2018, we and Dr. Frost entered into settlements with the SEC, which, upon approval by the court in January 2019, resolved the claims against us and Dr. Frost raised in the Complaint. Pursuant to the settlement between us and the SEC, and without admitting or denying any of the allegations of the Complaint, we agreed to an injunction from violations of Section 13(d) of the Securities Exchange Act of 1934 (the Exchange Act), a strict liability claim, and to pay a $100,000 penalty, which has been paid. We also agreed to, within certain stipulated time periods: (i) establish a Management Investment Committee (MIC) that will make recommendations to an Independent Investment Committee (IIC) of our Board of Directors in connection with existing and future strategic minority investments; and (ii) retain an Independent Compliance Consultant (ICC) to (a) advise us on whether filings pursuant to Section 13(d) of the Exchange Act for previous strategic investments made at the suggestion of or in tandem with Dr. Frost should be amended or made to reflect group membership with Dr. Frost and his related entities; (b) review our existing policies and procedures relating to compliance with Section 13(d) of the Exchange Act; and (c) review the independence of the MIC and IIC of our Board of Directors solely for purposes of the handling of strategic minority investments. The ICC is required to report its findings (including recommendations as to filings, amendments, improvements to policies and procedures, and improvement to the composition of the MIC and the IIC to our Board of Directors) to the SEC within 15 days of completion of its work, and we are required to implement the ICC s recommendations, and to certify our compliance with these undertakings in writing.

Under the terms of the settlement between the SEC and Dr. Frost, and without admitting or denying any of the allegations in the Complaint, Dr. Frost agreed to injunctions from violations of Sections 5(a) and (c) and 17(a)(2) of the Securities Act of 1933, as amended, (the Securities Act), claims which may be satisfied by strict liability and negligence, respectively, and Section 13(d) of the Exchange Act, also a strict liability claim; to pay approximately $5.5 million in penalty, disgorgement and pre-judgment interest, which has been paid; and to be prohibited, with certain exceptions, from trading in penny stocks.

The settlements include no restriction on Dr. Frost s ability to continue to serve as our CEO and Chairman.

We are separately evaluating our strategic minority investments and reporting under Section 13(d) of the Exchange Act. In connection with this evaluation, we may make additional or amended filings pursuant to Section 13(d) of the Exchange Act reflecting group membership.

Although the SEC matter against us and Dr. Frost is resolved, there can be no assurance that additional charges from other governmental authorities will not be brought against one or more parties named in the Complaint.

We also continue to face a number of class actions and derivative suits concerning the allegations in the SEC Complaint. We cannot predict with certainty the outcome or effect of the class actions or derivative suits, which could require us to pay substantial damages or could otherwise have a material adverse effect on us.

Our primary and side A directors and officers liability insurance carrier has denied coverage for the class action and derivative suits filed against us and our directors and officers concerning the allegations in the Complaint. We believe that this denial is in error and are in the process of appealing this coverage determination. If we are unsuccessful in this appeal, or if other third-party insurers deny, cancel, or refuse coverage, which we are not able to successfully appeal, or are otherwise unable to provide us with adequate insurance coverage for all or any of the aforementioned lawsuits, then our overall risk exposure and operational expenses could increase and the management of our business

operations could be disrupted, which could cause a material adverse impact on our business, operations and financial condition. Further, an unusually large liability claim or a string of

claims, like these lawsuits, could potentially exceed our available insurance coverage. In addition, the availability of, and our ability to collect on, insurance coverage can be subject to factors beyond our control.

As our current insurance policies expire, increased premiums for renewed or new coverage, if such coverage can be secured at all, may increase our insurance expense and/or require us to increase our self-insured retention or deductibles. If the number of claims or the dollar amounts of any such claims rise in any policy year, we could suffer additional costs associated with accessing excess coverage policies. Also, an increase in the loss amounts attributable to such claims could expose us to uninsured damages if we are unable or elect not to insure against certain claims because of increased premiums or other reasons. These lawsuits or the resolution of such lawsuits may affect the availability or cost of some of our insurance coverage, which could materially adversely impact our business, results of operations and cash flows and potentially expose us to increased risks that would be uninsured.

Adverse results in material litigation matters or governmental inquiries could have a material adverse effect upon our business and financial condition.

We may from time to time become subject in the ordinary course of business to material legal action related to, among other things, intellectual property disputes, professional liability, contractual and employee-related matters, as well as inquiries from governmental agencies and Medicare or Medicaid carriers requesting comment and information on allegations of billing irregularities and other matters that are brought to their attention through billing audits, third parties or other sources. The health care industry is subject to substantial federal and state government regulation and audit. Additionally, we are subject to pending legal proceedings with respect to alleged violations of securities laws. See Adverse results in material litigation matters or governmental inquiries could have a material adverse effect upon our business and financial condition above.

Legal actions could result in substantial monetary damages, negatively impact our ability to obtain additional funding on acceptable terms, or at all, and damage to our reputation with customers, business partners and other third parties, all of which could have a material adverse effect upon our results of operations and financial position. Further, the legal actions could damage our reputation with investors and adversely affect the trading prices of our securities.

Risks Related to Regulatory Compliance

Our ability to successfully operate our laboratories and develop and commercialize certain of our diagnostic tests and laboratory developed tests (LDTs) will depend on our ability to maintain required regulatory licensures and comply with all the CLIA requirements.

In order to successfully operate our laboratory business and offer certain of our diagnostic tests and LDTs, we must maintain our CLIA certification and comply with all the CLIA requirements. CLIA is designed to ensure the quality and reliability of clinical laboratories by mandating specific standards in the areas of personnel qualifications, administration and participation in proficiency testing, patient test management, quality control, quality assurance and inspections. The sanction for failure to comply with CLIA requirements may be suspension, revocation or limitation of a laboratory s CLIA certificate, which is necessary to conduct business, as well as significant fines and/or criminal penalties. Laboratories must undergo on-site surveys at least every two years, which may be conducted by the Federal CLIA program or by a private CMS-approved accrediting agency such as CAP, among others. Our laboratories are also subject to regulation of laboratory operations under state clinical laboratory laws as will be any new CLIA-certified laboratory that we establish or acquire. State clinical laboratory laws may require that laboratories and/or laboratory personnel meet certain qualifications, specify certain quality controls or require maintenance of certain records. Certain states, such as California, Florida, Maryland, New York, Pennsylvania and Rhode Island, require that laboratories obtain licenses to test specimens from patients residing in those states and additional states

may require similar licenses in the future. If we are unable to obtain and maintain licenses from states where required, we will not be able to process any samples

from patients located in those states. Only Washington and New York States are exempt under CLIA, as these states have established laboratory quality standards at least as stringent as CLIA s. Potential sanctions for violation of these statutes and regulations include significant fines and the suspension or loss of various licenses, certificates and authorizations, which could adversely affect our business and results of operations.

If we fail to comply with CLIA requirements, the U.S. Department of Health and Human Services (HHS) or state agencies could require us to cease diagnostic testing. Even if it were possible for us to bring our laboratories back into compliance after failure to comply with such requirements, we could incur significant expenses and potentially lose revenues in doing so. Moreover, new interpretations of current regulations or future changes in regulations under CLIA may make it difficult or impossible for us to comply with the CLIA classification, which would significantly harm our business and materially adversely affect our financial condition.

The regulatory approval process is expensive, time consuming and uncertain and may prevent us or our collaboration partners from obtaining approvals for the commercialization of some or all of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products, diagnostic products or medical devices are subject to extensive regulation by the FDA and other non-U.S. regulatory authorities, which regulations differ from country to country. In general, we are not permitted to market our product candidates in the U.S. until we receive approval of a BLA, an approval of a NDA, a clearance letter under the premarket notification process or 510(k) process, or an approval of a PMA from the FDA. To date, we have only submitted one NDA which was approved in June 2016. We have received FDA approval of the PMA for our Sangia Total PSA Test using the Claros Analyzer and a CE Mark for our *4KScore* test, but we have not received marketing approval or clearance for any of our other diagnostic product candidates. Obtaining approval of a NDA or PMA can be a lengthy, expensive and uncertain process. With respect to medical devices, while the FDA reviews and clears a premarket notification in as little as three months, there is no guarantee that our products will qualify for this more expeditious regulatory process, which is reserved for Class I and II devices, nor is there any assurance that even if a device is reviewed under the 510(k) process that the FDA will review it expeditiously or determine that the device is substantially equivalent to a lawfully marketed non-PMA device. If the FDA fails to make this finding, then we cannot market the device. In lieu of acting on a premarket notification, the FDA may seek additional information or additional data which would further delay our ability to market the product. Furthermore, we are not permitted to make changes to a device approved through the PMA or 510(k) which affects the safety or efficacy of the device without first submitting a supplement application to the PMA and obtaining FDA approval or cleared premarket notification for that supplement. In some cases, the FDA may require clinical trials to support a supplement application. In addition, failure to comply with FDA, non-U.S. regulatory authorities or other applicable U.S. and non-U.S. regulatory requirements may, either before or after product approval or clearance, if any, subject our company to administrative or judicially imposed sanctions, including, but not limited to the following:

- restrictions on the products, manufacturers or manufacturing process;
- adverse inspectional observations (Form 483), warning letters or non-warning letters incorporating inspectional observations;
- civil and criminal penalties;

injunctions;

suspension or withdrawal of regulatory approvals or clearances;

product seizures, detentions or import bans;

voluntary or mandatory product recalls and publicity requirements;

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total or partial suspension of production;

imposition of restrictions on operations, including costly new manufacturing requirements; and

refusal to approve or clear pending NDAs or supplements to approved NDAs, applications or pre-market notifications.

Regulatory approval of an NDA or NDA supplement, BLA, PMA, PMA supplement or clearance pursuant to a pre-market notification is not guaranteed, and the approval or clearance process, as the case may be, is expensive and may, especially in the case of an NDA or PMA application, take several years. The FDA also has substantial discretion in the drug and medical device approval and clearance process. Failure can occur at any stage, and we could encounter problems that cause us to abandon clinical trials or to repeat or perform additional pre-clinical studies and clinical trials. The number of pre-clinical studies and clinical trials that will be required for FDA approval or clearance varies depending on the drug or medical device candidate, the disease or condition that the drug or medical device candidate is designed to address, and the regulations applicable to any particular drug or medical device candidate. The FDA can delay, limit or deny approval or clearance of a drug or medical device candidate for many reasons, including:

a drug candidate may not be deemed safe or effective;

a medical device candidate may not be deemed to be substantially equivalent to a lawfully marketed non-PMA device, in the case of a premarket notification;

the FDA may not find the data from pre-clinical studies and clinical trials sufficient;

the FDA may not approve our or our third-party manufacturer s processes or facilities; or

the FDA may change its approval or clearance policies or adopt new regulations.

Beyond these risks, there is also a possibility that our licensees or collaborators could decide to discontinue a study at any time for commercial, scientific or other reasons.

Regulation by governmental authorities in the U.S. and other countries may be a significant factor in how we develop, test, produce and market our diagnostic test products. Diagnostic tests like ours may not fall squarely within the regulatory approval process for pharmaceutical or device products as described above, and the regulatory pathway is not as clear. It is possible that the diagnostic products developed by us or our collaborators will be regulated as medical devices by the FDA and comparable agencies of other countries and require either PMA or 510(k) clearance from the FDA prior to marketing. Some companies that have successfully commercialized diagnostic tests for various conditions and disease states have not sought clearance or approval for such tests through the traditional 510(k) or PMA processes, and have instead utilized a process involving LDTs through a CLIA- certified laboratory. CLIA is a federal law that regulates clinical laboratories that perform testing on specimens derived from humans for the purpose of providing information for diagnostic, preventative or treatment purpose. In such instances, the CLIA lab is solely

responsible for the development, validation and commercialization of the assay.

Such LDT testing is currently under the purview of CMS and state agencies that provide oversight of the safe and effective use of LDTs. However, the FDA has consistently asserted that it has the regulatory authority to regulate LDTs despite historically exercising enforcement discretion. In furtherance of that position, the FDA issued two draft guidance documents in October 2014: (1) Framework for Regulatory Oversight of Laboratory Developed Tests (the Framework Guidance); and (2) FDA Notification and Medical Device Reporting for Laboratory Developed Tests (the Notification Guidance). The Framework Guidance outlines the FDA s plan to adopt over time a risk-based approach to regulating LDTs whereby different classifications of LDTs would be subject to different levels of FDA oversight and enforcement, including, for example, prohibitions on adulteration and misbranding, establishment registration and device listing, premarket notification, banned devices, records and reports, good manufacturing practices, adverse event reporting, premarket review of safety,

effectiveness and clinical validity and quality system requirements. The Notification Guidance is intended to explain how clinical laboratories should notify the FDA of the LDTs they develop and how to satisfy Medical Device Reporting requirements. On January 13, 2017, the FDA published a synthesis of feedback on the Framework Guidance and Notification Guidance titled, Discussion Paper on Laboratory Developed Tests (the Discussion Paper). The Discussion Paper provided notice that the FDA would not issue a final guidance on the oversight of LDTs to allow for further public discussion on appropriate oversight approach, and to give congressional authorizing committees the opportunity to develop a legislative solution. The outcome and ultimate impact of such proposals on the business is difficult to predict at this time. However, the FDA s authority to regulate LDTs continues to be challenged and the regulatory situation is fluid. The timeline and process for finalizing the draft guidance documents is unknown. We will continue to monitor changes to all domestic and international LDT regulatory policy so as to ensure compliance with the current regulatory scheme.

The terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products and product candidates, which could materially impair our ability to generate anticipated revenues.

We, our approved or cleared products, and the manufacturers of our products are subject to continual review. Our approved or cleared products may only be promoted for their indicated uses. Marketing, labeling, packaging, adverse event reporting, storage, advertising and promotion for our approved products will be subject to extensive regulatory requirements. We train our marketing and sales force against promoting our products for uses outside of the cleared or approved indications for use, known as off-label uses. If the FDA determines that our promotional materials or training constitute promotion of unsupported claims or an off-label use, it could request that we modify our training or promotional materials or subject us to regulatory or enforcement actions, including the issuance of an untitled letter, a warning letter, injunction, seizure, civil fine or criminal penalties. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our business activities to constitute promotion of an off-label use, which could result in significant penalties, including, but not limited to, criminal, civil and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government healthcare programs and the curtailment of our operations.

We and the manufacturers of our products are also required to comply with cGMPs, regulations or the FDA s QSR regulations, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Moreover, device manufacturers are required to report adverse events by filing Medical Device Reports with the FDA, which reports are publicly available.

Further, regulatory agencies must approve manufacturing facilities before they can be used to manufacture our products, and these facilities are subject to ongoing regulatory inspection. If we fail to comply with the regulatory requirements of the FDA and other non-U.S. regulatory authorities, or if previously unknown problems with our products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions. Furthermore, any limitation on indicated uses for a product or product candidate or our ability to manufacture and promote a product or product candidate could significantly and adversely affect our business, results of operations and financial condition.

In addition, the FDA and other non-U.S. regulatory authorities may change their policies and additional regulations may be enacted that could prevent or delay marketing approval or clearance of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are not able to maintain regulatory compliance, we would likely not be permitted to market our products or product candidates and we may not achieve or sustain profitability, which would materially impair our ability to generate anticipated revenues.

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If we fail to comply with complex and rapidly evolving laws and regulations, we could suffer penalties, be required to pay substantial damages or make significant changes to our operations.

We are subject to numerous federal and state regulations, including, but not limited to:

- federal and state laws applicable to billing and claims payment;
- federal and state laboratory anti-mark-up laws;
- federal and state anti-kickback laws;
- physician self-referral law;
- federal and state false claims laws;
- federal self-referral and financial inducement prohibition laws, commonly known as the Stark Law, and the state equivalents;
- federal and state laws governing laboratory licensing and testing, including CLIA;
- federal and state laws governing the development, use and distribution of LDTs;
- HIPAA, along with the revisions to HIPAA as a result of the HITECH Act, and analogous state laws and non-US laws, including the General Data Protection Regulation;
- federal, state and foreign regulation of privacy, security, electronic transactions and identity theft;
- federal, state and local laws governing the handling, transportation and disposal of medical and hazardous waste;
- Occupational Safety and Health Administration rules and regulations;
- changes to laws, regulations and rules as a result of the implementation and/or repeal of part or all of 2010 Health Care Reform Legislation; and

changes to other federal, state and local laws, regulations and rules, including tax laws.

If we fail to comply with existing or future applicable laws and regulations, we could suffer civil or criminal penalties, including the loss of our licenses to operate our laboratories and our ability to participate in federal and state healthcare programs. Different interpretations and enforcement policies of existing statutes and regulations applicable to our business could subject our current practices to allegations of impropriety or illegality, or could require us to make significant changes to our operations. Under the federal False Claims Act (FCA), whistleblower or qui tam provisions allow a private individual to bring actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically and we may be subject to such suits. Violations of the FCA could result in enormous economic liability and could have a material impact on us. As a result of political, economic and regulatory influences, the healthcare delivery industry in the U.S. is under intense scrutiny and subject to fundamental changes. We cannot predict which reform proposals will be adopted, when they may be adopted or what impact they may have on us. The costs associated with complying with federal and state regulations could be significant and the failure to comply with any such legal requirements could have a material adverse effect on our financial condition, results of operations and liquidity.

Tax reform may significantly affect us and our stockholders.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act (the Tax Act) that significantly reforms the Internal Revenue Code of 1986, as amended. The Tax Act, among other things, includes changes to U.S. federal tax rates, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitations of the tax deduction for interest expense to 30% of adjusted earnings (except for

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certain small businesses), limitations of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, modifying or repealing many business deductions and credits and putting into effect the migration from a worldwide system of taxation to a territorial system.

Failure to maintain the security of patient-related information or compliance with security requirements could damage our reputation with customers, cause us to incur substantial additional costs and become subject to litigation.

Pursuant to HIPAA, and certain similar state laws, we must comply with comprehensive privacy and security standards with respect to the use and disclosure of protected health information. If we do not comply with existing or new laws and regulations related to protecting privacy and security of personal or health information, it could be subject to monetary fines, civil penalties or criminal sanctions. Under the HITECH amendments to HIPAA, HIPAA was expanded to require certain data breach notification, to extend certain HIPAA privacy and security standards directly to business associates, to heighten penalties for noncompliance and enhance enforcement efforts.

We may also be required to comply with the data privacy and security laws of other countries in which it operates or from which it receives data transfers. The European Union (EU) enacted the General Data Protection Regulation (GDPR) to replace the current data protection directive, Directive 95/46/EC, which took effect May 25, 2018, and which has a broader application and enhanced penalties for noncompliance. The GDPR, which is wide-ranging in scope, governs the collection and use of personal data in the EU and imposes operational requirements for companies that receive or process personal data of residents of the EU that are different than those currently in place in the EU. The GDPR will apply to our European operations and possibly to our laboratory and clinical development operations. We have implemented policies and procedures required to comply with the new EU regulations and will continue to evaluate compliance.

In March 2014, CareEvolve, BioReference s wholly-owned connectivity subsidiary, became aware that there had been a HIPAA breach with regard to one of its servers managed at an internet service provider site called XAND, where the server was inadvertently configured so that it was accessible to the Internet for a brief period. Upon becoming aware of the matter, CareEvolve immediately took the server offline and removed all indexed files that could be located on the internet. In the meantime, an Internet data collection robot operated by Google, Inc. had briefly acquired data from a server and made it available to Internet searches. To the best of our knowledge, there were no known disclosures of this Patient Health Information (PHI) to unauthorized parties. BioReference self-reported this incident to the appropriate government agency, the Office of Civil Rights (OCR). OCR notified BioReference that it has initiated an investigation of the breach report, and we are awaiting further discussion, investigation and action by OCR. Since March 2014, BioReference has taken meaningful steps to further improve its HIPAA and cybersecurity platform, including engaging independent and specialized IT consultants to conduct HIPAA and cybersecurity assessments, reviewing data security and internal safeguards and continuously implementing enhanced security measures to minimize the risk of similar occurrences in the future. We have had other data and security breaches in the ordinary course and such breaches may continue to happen from time to time despite our best efforts to prevent such breaches and safeguard private information. Some of these other data and security breaches have been reported to OCR and we are awaiting discussion, investigation or action by OCR. Any action by OCR may require us to pay fines or take remedial actions that may be expensive and require the attention of management, any of which may have a material adverse effect on us and our results of operations.

We have and will continue to receive certain personal and financial information about our clients and their patients. In addition, we depend upon the secure transmission of confidential information over public networks. While we take reasonable and prudent steps to protect this protected information, a compromise in our security

systems that results in client or patient personal information being obtained by unauthorized persons or our failure to comply with security requirements for financial transactions could adversely affect our reputation with our clients and result in litigation against us or the imposition of penalties, all of which may adversely impact our results of operations, financial condition and liquidity.

Failure to comply with environmental, health and safety laws and regulations, including the Federal Occupational Safety and Health Administration Act, the Needlestick Safety and Prevention Act and the Comprehensive Medical Waste Management Act, could result in fines and penalties and loss of licensure, and have a material adverse effect upon our business.

We are subject to licensing and regulation under federal, state and local laws and regulations relating to the protection of the environment and human health and safety, including laws and regulations relating to the handling, transportation and disposal of medical specimens, infectious and hazardous waste and radioactive materials, as well as regulations relating to the safety and health of laboratory employees. The Federal Occupational Safety and Health Administration has established extensive requirements relating to workplace safety for health care employers, including clinical laboratories, whose workers may be exposed to blood-borne pathogens such as HIV and the hepatitis B virus. These requirements, among other things, require work practice controls, protective clothing and equipment, training, medical follow-up, vaccinations and other measures designed to minimize exposure to, and transmission of, blood-borne pathogens. In addition, the Needlestick Safety and Prevention Act requires, among other things, that we include in our safety programs the evaluation and use of engineering controls such as safety needles if found to be effective at reducing the risk of needlestick injuries in the workplace.

Waste management is subject to federal and state regulations governing the transportation and disposal of medical waste including bodily fluids. Federal regulations require licensure of interstate transporters of medical waste. In New Jersey, we are subject to the Comprehensive Medical Waste Management Act which requires us to register as a generator of special medical waste. All of our medical waste is disposed of by a licensed interstate hauler. The hauler provides a manifest of the disposition of the waste products as well as a certificate of incineration, which is retained by us. These records are audited by the State of New Jersey on a yearly basis. We are also subject to the Federal Hazardous Materials Transportation Act, 49 U.S.C. 5101 et seq., and the Hazardous Materials Regulations (HMR), 49 CFR parts 171-180. The federal government has classified hazardous medical waste as hazardous materials for the purpose of regulation. These regulations preempt state regulation, which must be substantively the same, meaning that the non-federal requirement must conform in every significant respect to the federal requirement. Editorial and other similar de minimis changes are permitted, 49 CFR 107.202(d).

Failure to comply with such federal, state and local laws and regulations could subject us to denial of the right to conduct business, fines, criminal penalties and/or other enforcement actions, any of which could have a material adverse effect on our business. In addition, compliance with future legislation could impose additional requirements us, which may be costly.

Our failure or the failure of third-party payors or physicians to comply with ICD-10-CM Code Set, and our failure to comply with other emerging electronic transaction standards could adversely impact our business.

Compliance with the ICD-10-CM Code Set was required to be in place by October 1, 2015. We will continue our assessment of information systems, applications and processes for compliance with these requirements. Clinical laboratories are typically required to submit health care claims with diagnosis codes to third-party payors. The diagnosis codes must be obtained from the ordering physician for clinical laboratory testing and from the interpreting pathologist for anatomic pathology services. Our failure or the failure of third-party payors or physicians to comply with these requirements could have an adverse impact on reimbursement, days sales and cash collections.

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Also, the failure of our IT systems to keep pace with technological advances may significantly reduce our revenues or increase our expenses. Public and private initiatives to create healthcare information technology (HCIT) standards and to mandate standardized clinical coding systems for the electronic exchange of clinical information, including test orders and test results, could require costly modifications to our existing HCIT systems. If we fail to adopt or delay in implementing HCIT standards, we could lose customers and business opportunities.

Failure to comply with complex federal and state laws and regulations related to submission of claims for clinical laboratory services could result in significant monetary damages and penalties and exclusion from the Medicare and Medicaid programs.

We are subject to extensive federal and state laws and regulations relating to the submission of claims for payment for clinical laboratory services, including those that relate to coverage of our services under Medicare, Medicaid and other governmental health care programs, the amounts that may be billed for our services and to whom claims for services may be submitted. These rules may also affect us in light of the practice management products that we market, to the extent that these products are considered to affect the manner in which our customers submit their own claims for services. Submission of our claims is particularly complex because we provide both anatomic pathology services and clinical laboratory tests, which generally are paid using different reimbursement principles. The clinical laboratory tests are often paid under a clinical laboratory fee schedule, and the anatomic pathology services are often paid under a physician fee schedule.

Our failure to comply with applicable laws and regulations could result in our inability to receive payment for our services or result in attempts by third-party payors, such as Medicare and Medicaid, to recover payments from us that have already been made. Submission of claims in violation of certain statutory or regulatory requirements can result in penalties, including substantial civil money penalties for each item or service billed to Medicare in violation of the legal requirement, and exclusion from participation in Medicare and Medicaid. Government authorities may also assert that violations of laws and regulations related to submission or causing the submission of claims violate the FCA or other laws related to fraud and abuse, including submission of claims for services that were not medically necessary. Under the FCA, whistleblower or qui tam provisions allow a private individual to bring actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically and we may be subject to such suits. Violations of the FCA could result in enormous economic liability. The FCA provides that all damages are trebled, and each false claim submitted is subject to a penalty of up to $21,916. For example, we could be subject to FCA liability if it was determined that the services we provided were not medically necessary and not reimbursable, particularly if it were asserted that we contributed to the physician s referrals of unnecessary services to us. It is also possible that the government could attempt to hold us liable under fraud and abuse laws for improper claims submitted by an entity for services that we performed if we were found to have knowingly participated in the arrangement that resulted in submission of the improper claims.

Changes in regulation and policies, including increasing downward pressure on health care reimbursement, may adversely affect reimbursement for diagnostic services and could have a material adverse impact on our business.

Reimbursement levels for health care services are subject to continuous and often unexpected changes in policies, and we face a variety of efforts by government payors to reduce utilization and reimbursement for diagnostic testing services. Changes in governmental reimbursement may result from statutory and regulatory changes, retroactive rate adjustments, administrative rulings, competitive bidding initiatives and other policy changes.

The U.S. Congress has considered, at least yearly in conjunction with budgetary legislation, changes to one or both of the Medicare fee schedules under which we receive reimbursement, which include the physician fee

schedule for anatomical pathology services, and the clinical laboratory fee schedule for our clinical laboratory services. For example, currently there is no copayment or coinsurance required for clinical laboratory services, although there is for our services that are paid under the physician fee schedule. However, Congress has periodically considered imposing a 20 percent coinsurance on laboratory services. If enacted, this would require us to attempt to collect this amount from patients, although in many cases the costs of collection would exceed the amount actually received. In April 2015, changes to the physician fee schedule were enacted under the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA).

Our reimbursement for our pathology services is paid primarily under the physician fee schedule of Medicare and Medicaid. Historically, the physician fee schedule was governed by a complex formula, referred to as the Sustainable Growth Rate (SGR). However, in April 2015, MACRA was passed, which permanently replaces the SGR formula with a value-based payment system. The passage of MACRA also repealed the 21.1% reduction of the physician fee schedule that was scheduled for April 1, 2015. Under MACRA, the physician fee schedule conversion factor increases of 0.5% from July 1, 2015 to December 31, 2015, and 0.5% in each of years 2016-2019, followed by 0.0% updates for 2020-2025. Subsequent years will vary based on participation in alternative payment models. Beginning in 2019, rates were adjusted under the new Merit-based Incentive Payment System.

CMS pays laboratories on the basis of a fee schedule that is reviewed and re-calculated on an annual basis. CMS may change the fee schedule upward or downward on billing codes that we submit for reimbursement on a regular basis. Our revenue and business may be adversely affected if the reimbursement rates associated with such codes are reduced. Even when reimbursement rates are not reduced, policy changes add to our costs by increasing the complexity and volume of administrative requirements. Medicaid reimbursement, which varies by state, is also subject to administrative and billing requirements and budget pressures. Recently, state budget pressures have caused states to consider several policy changes that may impact our financial condition and results of operations, such as delaying payments, reducing reimbursement, restricting coverage eligibility and service coverage and imposing taxes on our services.

CMS has changed or discussed making changes to certain types of reimbursement which could affect our rate of reimbursement. Certain cases are comprised of both a technical component and a professional component. In certain specified areas of testing, primarily in the area of anatomic pathology, CMS has determined that some providers have over-utilized these testing procedures and CMS has introduced changes in reimbursement policies to discourage over-utilization. We are always subject to review by CMS and cannot be certain that CMS won t interpret our practices differently than we do.

Third-party payors are increasingly challenging established prices, and new products that are more expensive than existing treatments may have difficulty finding ready acceptance unless there is a clear therapeutic benefit. On April 1, 2014, the Protecting Access to Medicare Act of 2014 (PAMA) was enacted into law. Under PAMA, Medicare payment for clinical diagnostic laboratory tests is established by calculating a weighted mean of private payor rates. Effective January 1, 2018, clinical laboratory fee schedule rates will be based on weighted median private payor rates as required by PAMA. We cannot assure you that any of our products will be considered cost effective, or that reimbursement will be available or sufficient to allow us to sell them competitively and profitably.

The federal government is faced with significant economic decisions in the coming years. Some solutions being offered in the government could substantially change the way laboratory testing is reimbursed by government entities. We cannot be certain what or how any such government changes may affect our business.

Medicare legislation and future legislative or regulatory reform of the health care system may affect our ability to sell our products profitably.

In the U.S., there have been a number of legislative and regulatory initiatives, at both the federal and state government levels, to change the healthcare system in ways that, if approved, could affect our ability to sell our

products and provide our laboratory services profitably. As such, we cannot assure you that reimbursement payments under governmental and private third-party payor programs will remain at levels comparable to present levels or will be sufficient to cover the costs allocable to patients eligible for reimbursement under these programs. Any changes that lower reimbursement rates under Medicare, Medicaid or private payor programs could negatively affect our business.

Most significantly, on March 23, 2010, President Obama signed into law both the Affordable Care Act (the ACA) and the reconciliation law known as Health Care and Education Affordability Reconciliation Act (the Reconciliation Act and, collectively with the ACA, the 2010 Health Care Reform Legislation). The constitutionality of the 2010 Health Care Reform Legislation was confirmed on June 28, 2012 by the Supreme Court of the United States. However, as discussed in further detail below, the current Presidential administration has attempted to repeal and replace the 2010 Health Care Reform Legislation.

Beyond coverage and reimbursement changes, the 2010 Health Care Reform Legislation subjects manufacturers of medical devices to an excise tax of 2.3% on certain U.S. sales of medical devices beginning in January 2013. However, a two-year moratorium on the tax was issued on December 18, 2015. The moratorium was extended for an additional two-year period on January 22, 2018. As such, the excise tax does not apply to sales in 2016 through 2019. The return of the tax in January 2020 will likely increase our expense in the future.

Additionally, the 2010 Health Care Reform Legislation included significant fraud and abuse measures, including (i) required disclosures under the Open Payments Program (which implements the requirements of the Physician Payments Sunshine Act), which in conjunction with its implementing regulations, requires certain manufacturers of certain drugs, biologics and devices that are reimbursed by Medicare and Medicaid to report annually certain payments or transfers of value provided to physicians and teaching hospitals and to report annually ownership and investment interests held by physicians and their immediate family members during the preceding calendar year, (ii) lower thresholds for violations and (iii) increasing potential penalties for such violations. Federal funding available for combating health care fraud and abuse generally has increased. Many of the laws and regulations applicable to our business, particularly those relating to billing and reimbursement of tests and those relating to relationships with physicians, hospitals and patients, contain language that has not been interpreted by courts. We must rely on our interpretation of these laws and regulations based on the advice of our counsel and regulatory or law enforcement authorities may not agree with our interpretation of these laws and regulations and may seek to enforce legal remedies or penalties against us for violations. From time to time we may need to change our operations, particularly pricing or billing practices, in response to changing interpretations of these laws and regulations or regulatory or judicial determinations with respect to these laws and regulations. These occurrences, regardless of their outcome, could damage our reputation and harm important business relationships that we have with healthcare providers, payors and others. Furthermore, if a regulatory or judicial authority finds that we have not complied with applicable laws and regulations, we could be required to refund amounts that were billed and collected in violation of such laws and regulations. In addition, we may voluntarily refund amounts that were alleged to have been billed and collected in violation of applicable laws and regulations. In either case, we could suffer civil and criminal damages, fines and penalties, exclusion from participation in governmental healthcare programs and the loss of licenses, certificates and authorizations necessary to operate our business, as well as incur liabilities from third-party claims, all of which could harm our operating results and financial condition. Moreover, regardless of the outcome, if we or physicians or other third parties with whom we do business are investigated by a regulatory or law enforcement authority we could incur substantial costs, including legal fees, and our management may be required to divert a substantial amount of time to an investigation.

Prior to the 2016 U.S. elections (including the current Presidential administration), regulations under the 2010 Health Care Reform Legislation were expected to continue being drafted, released and finalized throughout the next several

years. In 2017, the President and members of Congress sought to repeal and replace the 2010 Health Care Reform Legislation. It is uncertain whether such repeal and replacement legislation will be enacted into law, and if enacted, what the impact might be on our business. It is also uncertain whether regulatory

changes to the implementation of the 2010 Health Care Reform Legislation will restrict patient access to affordable insurance and impact their access to novel, biosimilar and complex generic products. The full effects of any repeal and replacement of the 2010 Health Care Reform Legislation, or regulatory changes to its implementation, cannot be known until a new law is enacted or existing law is implemented through regulations or guidance issued by the CMS and other federal and state health care agencies. Because of the continued uncertainty about the implementation of the 2010 Health Care Reform Legislation, including the potential for further legal challenges or repeal of that legislation, we cannot quantify or predict with any certainty the likely impact of the 2010 Health Care Reform Legislation or its repeal on our business model, prospects, financial condition or results of operations. We also anticipate that Congress, state legislatures and third-party payors may continue to review and assess alternative healthcare delivery and payment systems and may in the future propose and adopt legislation or policy changes or implementations effecting additional fundamental changes in the healthcare delivery system. In addition, litigation may prevent some or all of the legislation from taking effect. We cannot assure you as to the ultimate content, timing or effect of changes, nor is it possible at this time to estimate the impact of any such potential legislation.

To enhance compliance with applicable health care laws, and mitigate potential liability in the event of noncompliance, regulatory authorities, such as the United States Health and Human Services Department Office of Inspector General (the OIG) have recommended the adoption and implementation of a comprehensive health care compliance program that generally contains the elements of an effective compliance and ethics program described in Section 8B2.1 of the United States Sentencing Commission Guidelines Manual, and for many years the OIG has made available a model compliance program targeted to the clinical laboratory industry (the Model Compliance Program). In addition, certain states, such as New York, require that health care providers, such as clinical laboratories, that engage in substantial business under the state Medicaid program have a compliance program that generally adheres to the standards set forth in the Model Compliance Program. Also, under the 2010 Health Care Reform Legislation, HHS requires suppliers, such as us, to adopt, as a condition of Medicare participation, compliance programs that meet a core set of requirements. While we have adopted U.S. healthcare compliance and ethics programs that generally incorporate the OIG s recommendations and train our employees in such compliance, having such a program can be no assurance that we will avoid any compliance issues.

Risks Related to International Operations

Failure to obtain regulatory approval outside the U.S. will prevent us from marketing our products and product candidates abroad.

We intend to market certain of our products and product candidates in non-U.S. markets. In order to market our products and product candidates in the EU and many other non-U.S. jurisdictions, we must obtain separate regulatory approvals. We have had limited interactions with non-U.S. regulatory authorities, the approval procedures vary among countries and can involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval or clearance. Approval or clearance by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more non-U.S. regulatory authority does not ensure approval by other regulatory authorities in other countries or by the FDA. The non-U.S. regulatory approval process may include all of the risks associated with obtaining FDA approval or clearance. We may not obtain non-U.S. regulatory approvals on a timely basis, if at all. We may not be able to file for non-U.S. regulatory approvals and may not receive necessary approvals to commercialize our products and product candidates in any market, which would have a material adverse effect on our business, results of operations and financial condition.

Non-U.S. governments often impose strict price controls, which may adversely affect our future profitability.

We intend to seek approval to market certain of our products and product candidates in both the U.S. and in non-U.S. jurisdictions. If we obtain approval in one or more non-U.S. jurisdictions, we will be subject to rules

and regulations in those jurisdictions relating to our product. In some countries, particularly countries of the EU, each of which has developed its own rules and regulations, pricing is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug or medical device candidate. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product and product candidates to other available products. If reimbursement of our products and product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to generate revenues and achieve or sustain profitability, which would have a material adverse effect on our business, results of operations and financial condition.

Potential political, economic and military instability in the State of Israel, where we have office, laboratory and manufacturing operations, may adversely affect our results of operations.

We maintain office, laboratory and manufacturing facilities in the State of Israel. Political, economic and military conditions in Israel may directly affect our ability to conduct business. Since the State of Israel was established in 1948, a number of armed conflicts have occurred between Israel and its neighbors. Any hostilities involving Israel or the interruption or curtailment of trade between Israel and its present trading partners, or a significant downturn in the economic or financial condition of Israel, could affect adversely our operations. Ongoing and revived hostilities or other Israeli political or economic factors could harm our operations and product development and cause our revenues to decrease.

Due to the international scope of our business activities, our results of operations may be significantly affected by currency fluctuations.

We derive a significant portion of our consolidated net revenues from international sales, subjecting us to risks relating to fluctuations in currency exchange rates. Currency variations can adversely affect margins on sales of our products in countries outside of the U.S. and margins on sales of products that include components obtained from suppliers located outside of the U.S. Through our subsidiaries, we operate in a wide variety of jurisdictions. Certain countries in which we operate or may operate have experienced geopolitical instability, economic problems and other uncertainties from time to time. To the extent that world events or economic conditions negatively affect our future sales to customers in these and other regions of the world, or the collectability of receivables, our future results of operations, liquidity and financial condition may be adversely affected. We may manage exposures arising in the normal course of business related to fluctuations in foreign currency exchange rates by entering into offsetting positions through the use of foreign exchange forward contracts. Certain firmly committed transactions are hedged with foreign exchange forward contracts whereby exchange rates change, gains and losses on the exposed transactions are partially offset by gains and losses related to the hedging contracts. However, our subsidiaries receive their income and pay their expenses primarily in their local currencies. To the extent that transactions of these subsidiaries are settled in their local currencies, a devaluation of those currencies versus the U.S. dollar could reduce the contribution from these subsidiaries to our consolidated results of operations as reported in U.S. dollars. For financial reporting purposes, such depreciation will negatively affect our reported results of operations since earnings denominated in foreign currencies would be converted to U.S. dollars at a decreased value. While we have employed economic cash flow and fair value hedges to minimize the risks associated with these exchange rate fluctuations, the hedging activities may be ineffective or may not offset more than a portion of the adverse financial impact resulting from currency variations. Accordingly, we cannot assure you that fluctuations in the values of the currencies of countries in which we operate will not materially adversely affect our future results of operations.

We may be exposed to liabilities under the Foreign Corrupt Practices Act (the FCPA), and any determination that we violated the FCPA could have a material adverse effect on our business.

We are subject to the FCPA and other laws that prohibit U.S. companies or their agents and employees from providing anything of value to a foreign official or political party for the purposes of influencing any act or

decision of these individuals in their official capacity to help obtain or retain business, direct business to any person or corporate entity or obtain any unfair advantage. We have operations and agreements with third parties and we generate sales internationally. Our international activities create the risk of unauthorized and illegal payments or offers of payments by our employees, consultants, sales agents or distributors, even though they may not always be subject to our control. We discourage these practices by our employees and agents. However, our existing safeguards and any future improvements may prove to be less than effective, and our employees, consultants, sales agents or distributors may engage in conduct for which we might be held responsible. Any failure by us to adopt appropriate compliance procedures and ensure that our employees and agents comply with the FCPA and applicable laws and regulations in foreign jurisdictions could result in substantial penalties or restrictions on our ability to conduct business in certain foreign jurisdictions.

Violations of the FCPA may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could negatively affect our business, operating results and financial condition. In addition, the U.S. government may seek to hold our Company liable for successor liability FCPA violations committed by companies in which we invest or that we acquire.

We are subject to risks associated with doing business globally.

Our operations, both within and outside the U.S., are subject to risks inherent in conducting business globally and under the laws, regulations and customs of various jurisdictions and geographies. These risks differ in some respects from those associated with our U.S. business and our exposure to such risks may increase if our international business continues to grow. These risks include fluctuations in currency exchange rates, changes in exchange controls, loss of business in government tenders that are held annually in many cases, nationalization, increasingly complex labor environments, expropriation and other governmental actions, changes in taxation, including legislative changes in U.S. and international taxation of income earned outside of the U.S., importation limitations, export control restrictions, violations of U.S. or local laws, including the FCPA, dependence on a few government entities as customers, pricing restrictions, economic destabilization, political and economic instability and disruption or destruction in a significant geographic region due to the location of manufacturing facilities, distribution facilities or customers, regardless of cause, including war, terrorism, riot, civil insurrection or social unrest or natural or man-made disasters, including famine, flood, fire, earthquake, storm or disease.

Our international business is subject to both U.S. and foreign laws and regulations, including, without limitation, regulations relating to import-export controls, technology transfer restrictions, repatriation of earnings, data privacy and protection, investment, exchange rates and controls, the FCPA and other anti-corruption laws, the anti-boycott provisions of the U.S. Export Administration Act, labor and employment, works councils and other labor groups, taxes, environment, security restrictions, intellectual property, changes in taxation, including legislative changes in U.S. and international taxation of income earned outside of the U.S., handling of regulated substances and other commercial activities. Failure by us, our employees, affiliates, partners or others with whom we work to comply with these laws and regulations could result in administrative, civil or criminal liabilities. New regulations and requirements, or changes to existing ones in the various countries in which we operate can significantly increase our costs and risks of doing business internationally. Failure to comply with the laws and regulations that affect our global operations, could have an adverse effect on our business, financial condition or results of operations.

Changes in regulations, political leadership and environment or security risks may dramatically affect our ability to conduct or continue to conduct business in international markets. Our international business may also be impacted by changes in foreign national policies and priorities, which may be influenced by changes in the environment, geopolitical uncertainties, government budgets and economic and political factors more generally, any of which could impact funding for programs or delay purchasing decisions or customer payments. We also could be affected by the

legal, regulatory and economic impacts of Britain s exit from the EU, the impact of which is not known at this time. The occurrence and impact of these factors is difficult to predict, but one or more of them could have a material adverse effect on our financial position, results of operations and/or cash flows.

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Risks Related to Acquisitions and Investments

Acquisitions, investments and strategic alliances that we have made or may make in the future may use significant resources, result in disruptions to our business or distractions of our management, may not proceed as planned and could expose us to unforeseen liabilities. We intend to continue to expand our business through the acquisition of, investments in and strategic alliances with companies, technologies, products and services. Acquisitions, investments and strategic alliances involve a number of special problems and risks, including, but not limited to:

- difficulty integrating acquired technologies, products, services, operations and personnel with the existing businesses;
- diversion of management s attention in connection with both negotiating the acquisitions and integrating the businesses;
- strain on managerial and operational resources as management tries to oversee larger operations and investments;
- difficulty implementing and maintaining effective internal control over financial reporting at businesses that we acquire or invest in, particularly if they are not located near our existing operations;
- exposure to unforeseen liabilities of acquired companies or companies in which we invest;
- potential costly and time-consuming litigation, including stockholder lawsuits;
- potential issuance of securities to equity holders of the company being acquired with rights that are superior to the rights of holders of our common stock, or which may have a dilutive effect on our stockholders;
- the need to incur additional debt or use cash; and
- the requirement to record potentially significant additional future operating costs for the amortization of intangible assets.

As a result of these or other problems and risks, businesses we acquire or invest in may not produce the revenues, earnings or business synergies that we anticipated, and acquired products, services or technologies might not perform as we expected. As a result, we may incur higher costs and realize lower revenues than we had anticipated. We may not be able to successfully address these problems and we cannot assure you that the acquisitions or investments will be successfully identified and completed or that, if completed, the acquired businesses, investments, products, services or technologies will generate sufficient revenue to offset the associated costs or other negative effects on our business.

Any of these risks can be greater if an acquisition or investment is large relative to our size. Failure to manage effectively our growth through acquisitions could adversely affect our growth prospects, business, results of operations, financial condition and cash flows.

We may fail to realize the anticipated benefits of the mergers with BioReference, Transition and other acquisitions.

The success of the mergers will depend on, among other things, our ability to combine our business with that of BioReference and Transition in a manner that facilitates growth opportunities and realizes synergies and cost savings. We believe that the mergers will provide an opportunity for revenue growth. However, we must successfully combine our business with that of BioReference and Transition in a manner that permits these benefits to be realized. In addition, we must achieve the anticipated growth and cost savings without adversely affecting current revenues and investments in future growth. If we are not able to successfully achieve these objectives, the anticipated benefits of the mergers may not be realized fully, or at all, or may take longer to realize than expected.

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The failure to integrate successfully the business and operations of BioReference in the expected time frame may adversely affect our future results.

Historically, we and BioReference have operated as independent companies. There can be no assurances that our and BioReference s businesses can be integrated successfully. It is possible that the integration process could result in the loss of our or BioReference s key employees, the loss of customers, the disruption of either company s or both companies ongoing businesses or in unexpected integration issues, higher than expected integration costs and an overall post-completion integration process that takes longer than originally anticipated. Specifically, the following issues, among others, must be addressed in integrating our operations with BioReference s operations in order to realize the anticipated benefits of the merger so we perform as expected:

- combining the companies operations and corporate functions, as well as obtaining anticipated synergies;
- combining our business with BioReference s business and meeting the capital requirements of the combined company, in a manner that permits us to achieve the cost savings or revenue synergies anticipated to result from the merger, the failure of which would result in the anticipated benefits of the merger not being realized in the time frame currently anticipated or at all;
- integrating the companies technologies;
- integrating and unifying the offerings and services available to customers;
- identifying and eliminating redundant and underperforming functions and assets;
- harmonizing and/or addressing differences in the companies operating practices, employee development and compensation programs, internal controls and other policies, procedures and processes;
- maintaining existing agreements with customers, distributors, providers and vendors and avoiding delays in entering into new agreements with prospective customers, distributors, providers and vendors;
- addressing possible differences in business backgrounds, corporate cultures and management philosophies;
- consolidating the companies administrative and information technology infrastructure;
- coordinating distribution and marketing efforts;

managing the movement of certain positions to different locations;

coordinating geographically dispersed organizations; and

effecting actions that may be required in connection with obtaining regulatory approvals.

In addition, at times the attention of our management and resources may be focused on the integration of the businesses of the two companies and diverted from day-to-day business operations, which may disrupt our ongoing business.

Funding may not be available for us to continue to make acquisitions, investments and strategic alliances in order to grow our business.

We have made and anticipate that we may continue to make acquisitions, investments and strategic alliances with complementary businesses, technologies, products and services to expand our business. Our growth plans rely, in part, on the successful completion of future acquisitions. At any particular time, we may need to raise substantial additional capital or to issue additional equity to finance such acquisitions, investments and strategic alliances. There is no assurance that we will be able to secure additional funding on acceptable terms, or at all, or obtain the stockholder approvals necessary to issue additional equity to finance such acquisitions, investments and strategic alliances. If we are unsuccessful in obtaining the financing, our business would be adversely impacted.

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We have a large amount of goodwill and other intangible assets as a result of acquisitions and have not yet tested goodwill for impairment as of October 1, 2018 or December 31, 2018. A significant write-down of goodwill and/or other intangible assets could have a material adverse effect on our reported results of operations and net worth and the trading prices of our securities.

We have a large amount of goodwill and other intangible assets. At September 30, 2018, we have goodwill and other intangible assets of $2.0 billion, or approximately 80% of our total assets, which exceeded our market cap on such date. Goodwill is tested at least annually for impairment or when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable, by assessing qualitative factors or performing a quantitative analysis in determining whether it is more likely than not that its fair value exceeds the carrying value. Examples of qualitative factors include our share price, our financial performance compared to budgets, long-term financial plans, macroeconomic, industry and market conditions as well as the substantial excess of fair value over the carrying value of net assets from the annual impairment test previously performed. The estimated fair value of a reporting unit is highly sensitive to changes in projections and assumptions; therefore, in some instances, changes in these assumptions could potentially lead to impairment. We perform sensitivity analyses around our assumptions in order to assess the reasonableness of the assumptions and the results of our testing. Ultimately, future potential changes in these assumptions may impact the estimated fair value of a reporting unit and cause the fair value of the reporting unit to be below its carrying value. We believe that our estimates are consistent with assumptions that marketplace participants would use in their estimates of fair value. However, if actual results are not consistent with our estimates and assumptions, we may be exposed to a non-cash impairment charge that could be material. We have not yet tested goodwill for impairment as of October 1, 2018 or December 31, 2018 and any goodwill impairment recorded as a result of such testing or any impairment charges in the future will adversely affect our results of operations. A significant write down of goodwill and/or other intangible assets could have a material adverse effect on our reported results of operations and net worth and the trading prices of our securities.

Risks Related to Ownership of Our Common Stock

The trading prices of our securities may fluctuate significantly.

The trading prices of our securities may fluctuate significantly in response to numerous factors, some of which are beyond our control, such as:

- the announcement of new products or product enhancements by us or our competitors;
- results of our clinical trials and other development efforts;
- developments concerning intellectual property rights and regulatory approvals;
- variations in our and our competitors results of operations;
- changes in earnings estimates or recommendations by securities analysts, if our common stock is covered by analysts;

developments in the biotechnology, pharmaceutical, diagnostic and medical device industry;

the announcement and/or commencement and/or settlement of lawsuits or similar claims against us or any of our officers, directors and affiliates;

the results of product liability or intellectual property lawsuits;

future issuances of our common stock or other securities, including debt;

purchases and sales of our common stock by our officers, directors or affiliates;

the addition or departure of key personnel;

announcements by us or our competitors of acquisitions, investments or strategic alliances; and

general market conditions and other factors, including factors unrelated to our operating performance.

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Further, the securities market in general, and the market for biotechnology, pharmaceutical, diagnostic and medical device companies in particular, has experienced extreme price and volume fluctuations in recent years. Continued market fluctuations could result in extreme volatility in the trading prices of our securities, which could cause a decline in the value of our securities.

Directors, executive officers, principal stockholders and affiliated entities own a substantial amount of our capital stock, and they may make decisions that you do not consider to be in the best interests of our stockholders.

As of January 28, 2019, our directors, executive officers, principal stockholders and affiliated entities beneficially owned, in the aggregate, approximately 44.2% of our outstanding voting securities. Phillip Frost, M.D., our Chairman and CEO, is deemed to beneficially own, in the aggregate, approximately 36.9% of our common stock as of January 28, 2019. As a result, Dr. Frost, acting with other members of management, would have the ability to significantly impact the election of our Board of Directors, the adoption or amendment of provisions in our Certificate of Incorporation, the approval of mergers and other significant corporate transactions and the outcome of issues requiring approval by our stockholders. This concentration of ownership may also have the effect of delaying or preventing a change in control of our company that may be favored by other stockholders. This could prevent transactions in which holders of our securities might otherwise recover a premium for their securities over current market prices.

A significant short position in our stock could have a substantial impact on the trading price of our stock.

Historically, there has been a significant short position in our common stock. As of December 31, 2018, investors held a short position of approximately 56,212,686 shares of our common stock which represented approximately 9.6% of our outstanding common stock. The anticipated downward pressure on our stock price due to actual or anticipated sales of our stock by some institutions or individuals who engage in short sales of our common stock could cause our stock price to decline. Such stock price decrease could encourage further short-sales that could place additional downward pressure on our stock price. This could lead to further increases in the already large short position in our common stock and cause volatility in our stock price.

The volatility of our stock may cause the value of a stockholder s investment to decline rapidly. Additionally, if our stock price declines, it may be more difficult for us to raise capital and may have other adverse effects on our business.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act, including with respect to companies we acquire, could have a material adverse effect on our business and operating results. In addition, current and potential holders of our securities could lose confidence in our financial reporting, which could have a material adverse effect on the trading prices of our securities.

Section 404 of the Sarbanes-Oxley Act of 2002 requires annual management assessments of the effectiveness of our internal control over financial reporting and a report by our independent registered public accounting firm on the effectiveness of internal control over financial reporting as of year-end. We are required to report, among other things, control deficiencies that constitute material weaknesses or changes in internal control that, or that are reasonably likely to, materially affect internal control over financial reporting. A material weakness is a significant deficiency or combination of significant deficiencies that results in more than a remote likelihood that a material misstatement of the annual or interim financial statements will not be prevented or detected.

We have identified and remediated control deficiencies in the past, and we cannot assure you that we will at all times in the future be able to report that our internal controls are effective. In addition, material weaknesses in the design

and operation of the internal control over financial reporting of companies that we acquire could have

a material adverse effect on our business and operating results. Our acquisition of BioReference and Transition and possible future acquisitions may increase this risk by expanding the scope and nature of operations over which we must develop and maintain internal control over financial reporting. If we cannot provide reliable financial reports or prevent fraud, our results of operation could be harmed. Our failure to maintain the effective internal control over financial reporting could cause the cost related to remediation to increase and could cause the trading prices of our securities to decline. In addition, we may not be able to accurately report our financial results, may be subject to regulatory sanction and investors may lose confidence in our financial statements.

Compliance with changing regulations concerning corporate governance and public disclosure may result in additional expenses.

There have been changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act, regulations promulgated by the SEC and rules promulgated by the Nasdaq Global Select Market and the other national securities exchanges. These new or changed laws, regulations and standards are subject to varying interpretations in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. As a result, our efforts to comply with evolving laws, regulations and standards are likely to continue to result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities. Our board members, CEO, Chief Financial Officer and Principal Accounting Officer could face an increased risk of personal liability in connection with the performance of their duties. As a result, we may have difficulty attracting and retaining qualified board members and executive officers, which could harm our business. If our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, we could be subject to liability under applicable laws or our reputation may be harmed, which could materially adversely affect our business, results of operations and financial condition.

Additional Risks Related to this Offering and the Notes

Although the notes are referred to as convertible senior notes, they will be effectively subordinated to any of our secured debt and any liabilities of our subsidiaries.

The notes will rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the notes; equal in right of payment to any of our liabilities that are not so subordinated; effectively junior in right of payment to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries. In the event of our bankruptcy, liquidation, reorganization or other winding up, our assets that secure debt ranking senior in right of payment to the notes will be available to pay obligations on the notes only after the secured debt has been repaid in full from these assets, and the assets of our subsidiaries will be available to pay obligations on the notes only after all claims senior to the notes have been repaid in full. There may not be sufficient assets remaining to pay amounts due on any or all of the notes then outstanding. The indenture governing the notes does not prohibit us from incurring additional senior debt or secured debt, nor does it prohibit any of our current or future subsidiaries from incurring additional liabilities.

As of September 30, 2018, we had $205.6 million of outstanding indebtedness for borrowed money (excluding intercompany debt). Our subsidiaries had $486.8 million of other liabilities (including trade payables but excluding intercompany obligations and liabilities of a type not required to be reflected on a balance sheet of such subsidiaries in accordance with U.S. GAAP). After giving effect to the issuance of the notes (assuming no exercise of the

underwriter s overallotment option to purchase additional notes), our and our subsidiaries indebtedness for borrowed money (excluding intercompany debt) would have been $405.6 million.

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The notes are our obligations exclusively and a substantial portion of our operations are conducted through, and a substantial portion of our consolidated assets are held by, our subsidiaries.

The notes are our obligations exclusively and are not guaranteed by any of our subsidiaries. A substantial portion of our consolidated assets are held by our subsidiaries. Accordingly, our ability to service our debt, including the notes, depends on the results of operations and cash flows of the consolidated company, including our subsidiaries and upon the ability of such subsidiaries to provide us with cash, whether in the form of dividends, loans or otherwise, to pay amounts due on our obligations, including the notes. Our subsidiaries are separate and distinct legal entities and have no obligation, contingent or otherwise, to make payments on the notes or to make any funds available for that purpose. In addition, dividends, loans or other distributions to us from such subsidiaries may be subject to contractual and other restrictions and are subject to other business considerations.

Recent and future regulatory actions and other events may adversely affect the trading price and liquidity of the notes.

We expect that many investors in, and potential purchasers of, the notes will employ, or seek to employ, a convertible arbitrage strategy with respect to the notes. Investors would typically implement such a strategy by selling short the common stock underlying the notes and dynamically adjusting their short position while continuing to hold the notes. Investors may also implement this type of strategy by entering into swaps on our common stock in lieu of or in addition to short selling the common stock.

The SEC and other regulatory and self-regulatory authorities have implemented various rules and taken certain actions, and may in the future adopt additional rules and take other actions, that may impact those engaging in short selling activity involving equity securities (including our common stock). Such rules and actions include Rule 201 of SEC Regulation SHO, the adoption by the Financial Industry Regulatory Authority, Inc. and the national securities exchanges of a Limit Up-Limit Down program, the imposition of market-wide circuit breakers that halt trading of securities for certain periods following specific market declines, and the implementation of certain regulatory reforms required by the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010. Any governmental or regulatory action that restricts the ability of investors in, or potential purchasers of, the notes to effect short sales of our common stock, borrow our common stock or enter into swaps on our common stock could adversely affect the trading price and the liquidity of the notes.

Volatility in the market price and trading volume of our common stock could adversely impact the trading price of the notes.

The stock market in recent years has experienced significant price and volume fluctuations that have often been unrelated to the operating performance of companies. The market price of our common stock could fluctuate significantly for many reasons, including in response to the risks described in this section, elsewhere in this prospectus supplement or the documents incorporated by reference in this prospectus supplement or for reasons unrelated to our operations, such as reports by industry analysts, investor perceptions or negative announcements by our customers, competitors or suppliers regarding their own performance, as well as industry conditions and general financial, economic and political instability. A decrease in the market price of our common stock would likely adversely impact the trading price of the notes. The price of our common stock could also be affected by possible sales of our common stock by investors who view the notes as a more attractive means of equity participation in us and by hedging or arbitrage trading activity that we expect to develop involving our common stock. This trading activity could, in turn, affect the trading prices of the notes.

We may not have sufficient cash flow from our business to service our indebtedness or pay our indebtedness.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, depends on our future performance, which is subject to economic, financial, competitive and other

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factors beyond our control. Our business may not continue to generate cash flow from operations in the future sufficient to service our indebtedness and make necessary capital expenditures. If we are unable to generate adequate cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring indebtedness or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default under our debt obligations, which could, in turn, adversely affect our business, financial condition and operating results.

We and our subsidiaries have a significant amount of debt and substantial debt service requirements, and we may still incur substantially more debt or take other actions, which would intensify the risks discussed above.

We and our subsidiaries have a significant amount of debt and substantial debt service requirements. This level of debt could have significant consequences on our future operations, including:

making it more difficult for us and our subsidiaries to meet our payment and other obligations;

our and our subsidiaries failure to comply with the financial and other restrictive covenants contained in our and their debt agreements, which could trigger events of default that could result in all of our or our subsidiaries debt becoming immediately due and payable;

reducing the availability of our and our subsidiaries cash flows to fund working capital, capital expenditures, acquisitions or strategic investments and other general corporate requirements, and limiting our and our subsidiaries ability to obtain additional financing for these purposes;

subjecting us and our subsidiaries to increased interest expense related to our and their indebtedness with variable interest rates, including borrowings under our credit facility;

limiting our and our subsidiaries flexibility in planning for, or reacting to, and increasing our vulnerability to changes in our business, the industry in which we operate and the general economy; and

placing us at a competitive disadvantage compared to our competitors that have less debt or are less leveraged.

In addition, we and our subsidiaries may incur substantial additional debt in the future, some of which may be secured debt. We will not be restricted under the terms of the indenture governing the notes from incurring additional debt, securing existing or future debt, recapitalizing our debt or taking a number of other actions that are not limited by the terms of the indenture governing the notes that could have the effect of diminishing our ability to make payments on the notes when due.

We may not have the ability to raise the funds necessary to settle conversions of the notes or to repurchase the notes upon a fundamental change, and our future debt may contain limitations on our ability to repurchase the notes.

Holders of the notes will have the right to require us to repurchase their notes upon the occurrence of a fundamental change at a repurchase price equal to 100% of their principal amount, plus accrued and unpaid interest, if any, as described under Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes. In addition, upon conversion of the notes, unless we elect to deliver solely shares of our common stock to settle such conversion (other than paying cash in lieu of delivering any fractional share), we will be required to make cash payments in respect of the notes being converted as described in under Description of Notes Conversion Rights Settlement upon Conversion. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of notes surrendered therefor or notes being converted.

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In addition, our ability to repurchase the notes or to pay cash upon conversion of the notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase or pay cash amounts due upon conversion of the notes as required would constitute a default under the indenture. A default under the indenture or the fundamental change itself could also lead to a default under agreements governing our future indebtedness. Moreover, the occurrence of a fundamental change under the indenture may constitute an event of default under agreements governing our future indebtedness. If the payment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the notes or to pay cash upon conversion of the notes.

Redemption may adversely affect your return on the notes.

We may not redeem the notes prior to February 15, 2022. We may redeem for cash any or all of the notes, at our option, on or after February 15, 2022, if the last reported price of our common stock has been at least 130% of the conversion price for the notes then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. As a result, we may choose to redeem the notes at times when prevailing interest rates are relatively low. As a result, you may not be able to reinvest the proceeds you receive from the redemption in a comparable security at an effective interest rate as high as the interest rate on your notes being redeemed. See Description of Notes Optional Redemption.

The conditional conversion feature of the notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional conversion feature of the notes is triggered, holders of notes will be entitled to convert the notes at any time during specified periods at their option. See Description of Notes Conversion Rights. If one or more holders elect to convert their notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our conversion obligation through the payment of cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

The accounting method for convertible debt securities that may be settled in cash, such as the notes, could have a material effect on our reported financial results.

Under Accounting Standards Codification 470-20, Debt with Conversion and Other Options, which we refer to as ASC 470-20, an entity must separately account for the liability and equity components of certain convertible debt instruments (such as the notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects the issuer s economic interest cost. The effect of ASC 470-20 on the accounting for the notes is that the equity component is required to be included in the additional paid-in capital section of stockholders equity on our consolidated balance sheet, and the value of the equity component is treated as original issue discount for purposes of accounting for the debt component of the notes. As a result, we expect that we will be required to record a greater amount of non-cash interest expense in current periods presented as a result of the amortization of the discounted carrying value of the notes to their respective face amounts over their respective terms. We expect that we will report lower net income in our financial results because ASC 470-20 will require interest to include both the current period s amortization of the debt discount and the instrument s coupon interest, which could adversely affect our financial

results, the trading price of our common stock and the trading price of the notes.

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In addition, under certain circumstances, convertible debt instruments (such as the notes) that may be settled entirely or partly in cash are currently accounted for utilizing the treasury stock method, the effect of which is that any shares issuable upon conversion of the notes are not included in the calculation of diluted earnings per share except to the extent that the conversion value of the notes exceeds their respective principal amounts. Under the treasury stock method, for diluted earnings per share purposes, the transaction is accounted for as if the number of shares of common stock that would be necessary to settle such excess, if we elected to settle such excess in shares, are issued. We cannot be sure that the accounting standards in the future will continue to permit the use of the treasury stock method. If we are unable to use the treasury stock method in accounting for the shares issuable upon conversion of the notes, then our diluted earnings per share would be adversely affected.

Future sales of our common stock, as well as sales of the borrowed shares in the concurrent offering, or the issuance of other equity-related securities could lower the market price for our common stock and adversely impact the trading price of the notes.

In the future, we may sell additional shares of our common stock or other equity-related securities. In addition, a substantial number of shares of our common stock are reserved for issuance upon the exercise of stock options pursuant to our equity benefit plans, warrants to purchase shares of our common stock, upon conversion of the 2033 Senior Notes, the 2023 Convertible Notes, in each case as defined below, and upon conversion of the notes offered hereby. We cannot predict the size of future issuances or the effect, if any, that they may have on the market price for our common stock. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the trading price of the notes and the market price of our common stock and impair our ability to raise capital through the sale of additional equity or equity-related securities.

Concurrently with this offering and by means of a separate prospectus supplement and accompanying prospectus, up to 30,000,000 of shares of our common stock will be offered by selling stockholders, who will borrow such shares through lending arrangements from an affiliate of the underwriter, which is borrowing the shares, as Share Borrower, from us. We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their investments in the notes. The selling stockholders may effect such transactions by selling the borrowed shares at various prices from time to time through the Share Borrower or its affiliates. The selling stockholders will receive all of the net proceeds from the sale of the borrowed shares, and we will not receive any of those proceeds, but we will receive from the Share Borrower a one-time nominal fee of $0.01 per share for each newly issued share. Pursuant to a share lending agreement between us and the Share Borrower, the Share Borrower has agreed to pay us an amount of cash equal to the aggregate dividend paid for any cash dividend or distribution we make in respect of the borrowed shares.

All borrowed shares (or identical shares or, in certain circumstances, the cash value thereof) must be returned to us on or about the maturity date of the notes or, if earlier, on or about the date as of which all of the notes cease to be outstanding as a result of redemption, repurchase, conversion or other acquisition for value (or earlier in certain other circumstances). See Description of Share Lending Agreement. The existence of these arrangements, the short sales of shares of our common stock effected in connection with the sale of the notes or any unwind of such short sales could cause the market price of our common stock to be lower over the term of these arrangements than it otherwise would have been, due to the effect of the increase in the number of outstanding shares of our common stock being traded in the market or otherwise.

The adjustments by holders of the notes of their hedging positions in shares of our common stock and the expectation thereof may have a negative effect on the market price of our common stock.

The short positions in shares of our common stock resulting from the share lending arrangements and the sale of borrowed shares in the concurrent offering are expected to be used by the Share Borrower to facilitate hedging, including through short sales of shares of our common stock, by holders of the notes. The borrowed shares sold in the concurrent offering may be more or less than the number of shares that will be needed from

time to time by the holders of the notes to hedge their exposure under the notes. Any buying or selling of shares of our common stock by the holders of the notes to adjust their hedging positions may affect the market price of our common stock.

Changes in the accounting guidelines relating to the borrowed shares sold in the concurrent offering could decrease our reported net loss or earnings per share and potentially affect the price of our common stock.

Because the amount of borrowed shares sold in the concurrent offering (or in certain circumstances, the cash value thereof) must be returned to us upon the expiration or early termination of the share lending arrangements pursuant to their terms, we believe that under U.S. GAAP, as presently in effect, the borrowed shares will not be considered outstanding for the purpose of computing and reporting our earnings or loss per share. If accounting guidelines were to change in the future, we may become required to treat the borrowed shares as outstanding for purposes of computing earnings or loss per share, and our reported earnings or net loss per share would be reduced, which could affect the market price of our common stock.

Holders of notes will not be entitled to any rights with respect to our common stock, but they will be subject to all changes made with respect to them to the extent our conversion obligation includes shares of our common stock.

Holders of notes will not be entitled to any rights with respect to our common stock (including, without limitation, voting rights and rights to receive any dividends or other distributions on our common stock) prior to the conversion date relating to such notes (if we have elected to settle the relevant conversion by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share)) or the last trading day of the relevant observation period (if we elect to pay and deliver, as the case may be, a combination of cash and shares of our common stock in respect of the relevant conversion), but holders of notes will be subject to all changes affecting our common stock. For example, if an amendment is proposed to our certificate of incorporation or bylaws requiring stockholder approval and the record date for determining the stockholders of record entitled to vote on the amendment occurs prior to the conversion date related to a holder s conversion of its notes (if we have elected to settle the relevant conversion by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share)) or the last trading day of the relevant observation period (if we elect to pay and deliver, as the case may be, a combination of cash and shares of our common stock in respect of the relevant conversion), such holder will not be entitled to vote on the amendment, although such holder will nevertheless be subject to any changes affecting our common stock.

The conditional conversion feature of the notes could result in your receiving less than the value of our common stock into which the notes would otherwise be convertible.

Prior to the close of business on the business day immediately preceding November 15, 2024, you may convert your notes only if specified conditions are met. If the specific conditions for conversion are not met, you will not be able to convert your notes, and you may not be able to receive the value of the cash, common stock or a combination of cash and common stock, as applicable, into which the notes would otherwise be convertible.

Upon conversion of the notes, you may receive less valuable consideration than expected because the value of our common stock may decline after you exercise your conversion right but before we settle our conversion obligation.

Under the notes, a converting holder will be exposed to fluctuations in the value of our common stock during the period from the date such holder surrenders notes for conversion until the date we settle our conversion obligation.

Upon conversion of the notes, we have the option to pay or deliver, as the case may be, cash, shares of our common stock, or a combination of cash and shares of our common stock. If we elect to satisfy our conversion

obligation in cash or a combination of cash and shares of our common stock, the amount of consideration that you will receive upon conversion of your notes will be determined by reference to the volume-weighted average prices of our common stock for each trading day in a 25 trading-day observation period. As described under Description of Notes Settlement upon Conversion, this period would be (i) subject to clause (ii), if the relevant conversion date occurs prior to November 15, 2024, the 25 consecutive trading day period beginning on, and including, the second trading day after such conversion date; (ii) if the relevant conversion date occurs on or after the date of our issuance of a notice of redemption as described under Description of Notes Optional Redemption and prior to the relevant redemption date, the 25 consecutive trading days beginning on, and including, the 26th scheduled trading day immediately preceding such redemption date; and (iii) subject to clause (ii), if the relevant conversion date occurs on or after November 15, 2024, the 25 consecutive trading days beginning on, and including, the 26th scheduled trading day immediately preceding February 15, 2025. Accordingly, if the price of our common stock decreases during this period, the amount and/or value of consideration you receive will be adversely affected. In addition, if the market price of our common stock at the end of such period is below the average of the volume-weighted average price of our common stock during such period, the value of any shares of our common stock that you will receive in satisfaction of our conversion obligation will be less than the value used to determine the number of shares that you will receive.

If we elect to satisfy our conversion obligation solely in shares of our common stock upon conversion of the notes, we will be required to deliver the shares of our common stock, together with cash for any fractional share, on the second business day following the relevant conversion date (provided that, with respect to any conversion date occurring after November 15, 2024, settlement will occur on the maturity date of the notes). Accordingly, if the price of our common stock decreases during this period, the value of the shares that you receive will be adversely affected and would be less than the conversion value of the notes on the conversion date.

The notes are not protected by restrictive covenants.

The indenture governing the notes does not contain any financial or operating covenants or restrictions on the payments of dividends, the incurrence of indebtedness or the issuance or repurchase of securities by us or any of our subsidiaries. The indenture contains no covenants or other provisions to afford protection to holders of the notes in the event of a fundamental change or other corporate transaction involving us except to the extent described under Description of Notes Fundamental Change Permits Holders to Require Us to Repurchase Notes, Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption and Description of Notes Consolidation, Merger or Sale of Assets.

The increase in the conversion rate for notes converted in connection with a make-whole fundamental change or redemption may not adequately compensate you for any lost value of your notes as a result of such transaction.

If a make-whole fundamental change or redemption occurs prior to the maturity date, under certain circumstances, we will increase the conversion rate by a number of additional shares of our common stock for notes converted in connection with such make-whole fundamental change or redemption, as applicable. The increase in the conversion rate will be determined based on the date on which the specified corporate transaction becomes effective or the date of the redemption notice, as the case may be, and the price paid (or deemed to be paid) per share of our common stock in such transaction, as described below under Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption. The increase in the conversion rate for notes converted in connection with a make-whole fundamental change or redemption, as applicable, may not adequately compensate you for any lost value of your notes as a result of such transaction or in connection with the redemption, as applicable. In addition, if the price of our common stock in the transaction or in connection with the redemption is greater than $25.00 per share or less than $3.52 per share (subject to adjustment), no additional shares will be added to the conversion rate. Moreover, in no event will the conversion rate per $1,000

principal amount of notes as a result

of this adjustment exceed 284.0909 shares of common stock, subject to adjustment in the same manner as the conversion rate as set forth under Description of Notes Conversion Rights Conversion Rate Adjustments.

Our obligation to increase the conversion rate for notes converted in connection with a make-whole fundamental change or redemption could be considered a penalty, in which case the enforceability thereof would be subject to general principles of reasonableness and equitable remedies.

Upon any optional redemption of the notes or any conversion of the notes in connection with a related redemption notice, the cash comprising the redemption price, in the case of an optional redemption, or the applicable conversion rate, in the case of a conversion in connection with a redemption notice, as applicable, may not fully compensate you for future interest payments or lost time value of your notes.

On or after February 15, 2022, we may redeem for cash any or all of the notes, at our option, if the last reported sale price of our common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive), during any 30 consecutive trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. If we call the notes for optional redemption, you may convert all or any portion of your notes at any time prior to the close of business on the scheduled trading day immediately preceding the redemption date. Upon such redemption or conversion, the cash comprising the redemption price, in the case of an optional redemption, or the applicable conversion rate, in the case of a conversion in connection with a related redemption notice, in either case, may not fully compensate you for any future interest payments that you would have otherwise received or any other lost time value of your notes. See Description of Notes Optional Redemption.

The conversion rate of the notes may not be adjusted for all dilutive events.

The conversion rate of the notes is subject to adjustment for certain events, including, but not limited to, the issuance of certain stock dividends on our common stock, the issuance of certain rights or warrants, subdivisions, combinations, distributions of capital stock, indebtedness, or assets, cash dividends and certain issuer tender or exchange offers as described under Description of Notes Conversion Rights Conversion Rate Adjustments. However, the conversion rate will not be adjusted for other events, such as a third-party tender or exchange offer or an issuance of common stock for cash, that may adversely affect the trading price of the notes or our common stock. An event that adversely affects the value of the notes may occur, and that event may not result in an adjustment to the conversion rate.

Provisions in the indenture for the notes may deter or prevent a business combination that may be favorable to you.

If a fundamental change occurs prior to the maturity date of the notes, holders of the notes will have the right, at their option, to require us to repurchase all or a portion of their notes. In addition, if a make-whole fundamental change occurs prior to the maturity date of the notes, we will in some cases be required to increase the conversion rate for a holder that elects to convert its notes in connection with such fundamental change. Furthermore, the indenture for the notes prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the notes. These and other provisions in the indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to you.

Some significant restructuring transactions may not constitute a fundamental change, in which case we would not be obligated to offer to repurchase the notes.

Upon the occurrence of a fundamental change, you have the right to require us to repurchase your notes. However, the fundamental change provisions will not afford protection to holders of notes in the event of other

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transactions that could adversely affect the notes. For example, transactions such as leveraged recapitalizations, refinancings, restructurings, or acquisitions initiated by us may not constitute a fundamental change requiring us to repurchase the notes. In the event of any such transaction, the holders would not have the right to require us to repurchase the notes, even though each of these transactions could increase the amount of our indebtedness, or otherwise adversely affect our capital structure or any credit ratings, thereby adversely affecting the holders of notes.

We cannot assure you that an active trading market will develop for the notes.

Prior to this offering, there has been no trading market for the notes, and we do not intend to apply to list the notes on any securities exchange or to arrange for quotation on any automated dealer quotation system. We have been informed by the underwriter that it intends to make a market in the notes after the offering is completed. However, the underwriter may cease its market-making at any time without notice. In addition, the liquidity of the trading market in the notes, and the market price quoted for the notes, may be adversely affected by changes in the overall market for this type of security and by changes in our financial performance or prospects or in the prospects for companies in our industry generally. As a result, we cannot assure you that an active trading market will develop for the notes. If an active trading market does not develop or is not maintained, the market price and liquidity of the notes may be adversely affected. In that case you may not be able to sell your notes at a particular time or you may not be able to sell your notes at a favorable price.

Any adverse rating of the notes may cause their trading price to fall.

We do not intend to seek a rating on the notes. However, if a rating service were to rate the notes and if such rating service were to lower its rating on the notes below the rating initially assigned to the notes or otherwise announces its intention to put the notes on credit watch, the trading price of the notes could decline.

You may be subject to tax if we make or fail to make certain adjustments to the conversion rate of the notes even though you do not receive a corresponding cash distribution.

The conversion rate of the notes is subject to adjustment in certain circumstances, including the payment of cash dividends. If the conversion rate is adjusted as a result of a distribution that is taxable to our common stockholders, such as a cash dividend, you may be deemed to have received a dividend subject to U.S. federal income tax without the receipt of any cash. In addition, a failure to adjust (or to adjust adequately) the conversion rate after an event that increases your proportionate interest in us could be treated as a deemed taxable dividend to you. If a make-whole fundamental change or redemption, as the case may be, occurs on or prior to the maturity date of the notes, under some circumstances, we will increase the conversion rate for notes converted in connection with the make-whole fundamental change or during the related redemption period. Such increase may also be treated as a distribution subject to U.S. federal income tax as a dividend. See U.S. Federal Income Tax Considerations. If you are a non-U.S. holder (as defined under U.S. Federal Income Tax Considerations), any deemed dividend would generally be subject to U.S. federal withholding tax at a 30% rate, or such lower rate as may be specified by an applicable treaty, which may be set off against subsequent payments on the notes (including upon conversion, repayment or maturity), or in some circumstances from any payments on our common stock or from sales proceeds subsequently paid or credited to you, or from your other funds or assets. See U.S. Federal Income Tax Considerations.

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CAUTIONARY STATEMENT ABOUT FORWARD-LOOKING INFORMATION

This prospectus supplement, the accompanying prospectus and the documents and information incorporated by reference herein and therein may contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Forward-looking statements may include, but are not limited to, statements relating to our objectives, plans and strategies as well as statements, other than historical facts, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future. These statements are often characterized by terminology such as may, will, should, expects, plans, anticipates, intends, target, projects, contemplates, believes, estimates, predicts, potential, or continue or the neg terms or other similar expressions.

Forward-looking statements are based on assumptions and assessments made in light of our experience and perception of historical trends, current conditions, expected future developments and other factors believed to be appropriate. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties, many of which are outside of our control. You should not place undue reliance on these forward-looking statements, which reflect our view only as of the date of this prospectus supplement, and we undertake no obligation to update these forward-looking statements in the future, except as required by applicable law.

A number of important factors could cause actual results to differ materially from those indicated by the forward-looking statements, including, without limitation, those factors described under the caption Risk Factors in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, which is incorporated by reference in this prospectus supplement and the accompanying prospectus, and under similar headings in our subsequently filed quarterly reports on Form 10-Q, as well as the other risks and uncertainties described herein and in the other documents incorporated by reference in this prospectus supplement. Some of the key factors that could cause actual results to differ from our expectations include the following:

- we have a history of losses and may not generate sustained positive cash flow sufficient to fund our operations and research and development programs;
- our need for, and ability to obtain, additional financing when needed on favorable terms, or at all;
- adverse results in material litigation matters or governmental inquiries, including, without limitation, recent lawsuits against us and our Chairman and CEO by the SEC, as well as related class action and derivative lawsuits;
- the risks inherent in developing, obtaining regulatory approvals for, and commercializing new, commercially viable and competitive products and treatments;
- our research and development activities may not result in commercially viable products;
- that earlier clinical results of effectiveness and safety may not be reproducible or indicative of future results;

the success of our relationship with Pfizer;

that we may fail to obtain regulatory approval for hGH-CTP or successfully commercialize *Rayaldee* and hGH-CTP;

that we may not generate profits or cash flow from our laboratory operations or substantial revenue from *Rayaldee* and our pharmaceutical and diagnostic products;

that currently available over-the-counter and prescription products, as well as products under development by others, may prove to be as or more effective than our products for the indications being studied;

our ability to build a successful pharmaceutical sales and marketing infrastructure;

our ability and our distribution and marketing partners ability to comply with regulatory requirements regarding the sales, marketing and manufacturing of our products and product candidates and the operation of our laboratories;

the performance of our third-party distribution partners, licensees and manufacturers over which we have limited control;

our success is dependent on the involvement and continued efforts of our Chairman and CEO;

integration challenges for Transition, BioReference Laboratories or BioReference, EirGen and other acquired businesses;

availability of insurance coverage with respect to material litigation matters;

changes in regulation and policies in the U.S. and other countries, including increasing downward pressure on healthcare reimbursement;

our ability to manage our growth and our expanded operations;

increased competition, including price competition;

changing relationships with payors, including the various state and multi-state Blues programs, suppliers and strategic partners;

efforts by third-party payors to reduce utilization and reimbursement for clinical testing services;

our ability to maintain reimbursement coverage for our products and services, including the *4Kscore* test;

failure to timely or accurately bill and collect for our services;

failure in our information technology systems, including cybersecurity attacks or other data security or privacy incidents;

failure to obtain and retain new clients and business partners, or a reduction in tests ordered or specimens submitted by existing clients;

failure to establish, and perform to, appropriate quality standards to assure that the highest level of quality is observed in the performance of our testing services;

failure to maintain the security of patient-related information;

our ability to obtain and maintain intellectual property protection for our products;

our ability to defend our intellectual property rights with respect to our products;

our ability to operate our business without infringing the intellectual property rights of others;

our ability to attract and retain key scientific and management personnel;

failure to obtain and maintain regulatory approval outside the U.S.;

legal, economic, political, regulatory, currency exchange and other risks associated with international operations; and

our ability to finance and successfully complete construction of a research, development and manufacturing center in Waterford, Ireland.

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USE OF PROCEEDS

We estimate that the net proceeds to us from this offering of notes will be approximately $192.3 million (or $221.3 million if the underwriter exercises its over-allotment option in full), after deducting the underwriter s discount and commission and our estimated expenses relating to the offering.

We intend to use the net proceeds we receive from sales of securities offered hereby to fund research and development to further develop and commercialize our portfolio of proprietary pharmaceutical and diagnostic products and for working capital, capital expenditures, acquisitions and other general corporate purposes, which will include the repayment or repurchase of indebtedness or debt securities outstanding from time to time, including $28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit with an affiliate of Dr. Frost.

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DIVIDEND POLICY

We have not declared or paid any cash dividends on our common stock and do not intend to pay cash dividends on our common stock in the near future.

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CAPITALIZATION

The following table sets forth our cash and cash equivalents and consolidated capitalization as of September 30, 2018:

on an actual basis reflecting our consolidated cash and cash equivalents and capitalization; and

on an as-adjusted basis reflecting our consolidated cash and cash equivalents and capitalization to give effect to this offering and the use of the net proceeds from this offering.

The information in this table should be read in conjunction with Use of Proceeds, included elsewhere in this prospectus supplement, and Management s Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and the related notes contained in our Form 8-K filed with the SEC on January 28, 2019 and our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2018, which are incorporated by reference into this prospectus supplement and the accompanying prospectus, as well as the other financial information incorporated by reference into this prospectus supplement and the accompanying prospectus.

	As of September 30, 2018	
	Actual	As Adjusted
	(unaudited) (in millions)	
Cash and Cash Equivalents	$ 43.7	$ 207.2(6)
Debt:		
4.5% Convertible Senior Notes Due 2025 offered hereby(1)		192.3
3.0% Senior Notes Due 2033(2)	31.0	3.1
5.0% Convertible Promissory Notes due 2023(3)	56.6	56.6
BioReference Credit Agreement(4)	105.0	105.0
Other local lines of credit	4.7	4.7
Other indebtedness	8.3	8.3
Total	$ 205.6	$ 370.0
Equity:		
Common shares, par value $0.01 per share; 750,000,000 shares authorized; 560,377,422 shares issued at September 30, 2018(5)	$ 5.6	$ 5.6
Treasury Stock 549,907 shares at September 30, 2018	(1.8)	(1.8)
Additional paid-in capital	2,907.0	2,907.0
Accumulated other comprehensive loss	(13.1)	(13.1)
Accumulated deficit	(1,109.0)	(1,109.0)
Total shareholders equity	$ 1,789.0	$ 1,789.0
Total capitalization	$ 1,994.6	$ 2,159.0

(1) In accordance with Financial Accounting Standards Board Accounting Standards Codification 470-20, Debt with Conversion and Other Options (ASC 470-20), convertible debt that may be entirely or partially, settled in cash (such as the notes) is required to be separated into a liability and an equity component, such that interest expense reflects the issuer s non-convertible debt interest cost. We expect that on the issuance date, the value of the conversion option of the notes, representing the equity component, will be recorded as additional paid-in capital within stockholders equity and as an original issue discount to the notes, which reduces their initial carrying value. We expect that the carrying value of the notes, net of the discount recorded, will be accreted up to the principal amount of the notes from the issuance date until maturity. ASC 470-20 does not affect the actual amount that we are required to repay. The amount shown in the table above for the notes is the aggregate principal amount of the notes, without reflecting the debt discount for the value of the conversion option, and is net of the underwriters discounts and our estimated offering expenses related to this offering.

(2) Holders of the 2033 Senior Notes may require us to repurchase the 2033 Senior Notes for 100% of their principal amount, plus accrued and unpaid interest, on February 1, 2019, February 1, 2023 and February 1, 2028 under the indenture governing the 2033 Senior Notes. We anticipate using a portion of the net proceeds of this offering to repurchase such amount of 2033 Senior Notes as we were required to repurchase on February 1, 2019 pursuant to the terms of the indenture governing the 2033 Senior Notes. On February 1, 2019, approximately $28.8 million aggregate principal amount of 2033 Senior Notes were tendered by holders thereof pursuant to such holders option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes. The aggregate repurchase price for such 2033 Senior Notes was the aggregate principal amount of such 2033 Senior Notes, plus accrued and unpaid interest thereon to, but not including, the date of repurchase. Following the repurchase, approximately $3.1 million aggregate principal amount of the 2033 Senior Notes will remain outstanding, as reflected in the As Adjusted column.

(3) The amount shown in the table above for the notes is the aggregate principal amount of the notes, including accrued interest.

(4) As of September 30, 2018, the total availability under the Credit Agreement with CB and our lines of credit with financial institutions in Chile and Spain was $138.0 million, of which $109.7 million was used and outstanding as of September 30, 2018. The weighted average interest rate on these lines of credit is approximately 4.7%. See Description of Other Indebtedness .

(5) Does not include 33,011,848 shares of our common stock issuable under our stock option plans based on outstanding awards as of September 30, 2018 or up to 644,330 shares of our common stock that may be issuable to the sellers of Claros Diagnostics Inc. in connection with the approval of the Sangia Total PSA Test using the Claros Analyzer.

(6) Reflects the use of proceeds to repay $28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit with an affiliate of Dr. Frost as described in Subsequent Events below.

Subsequent Events

On November 8, 2018, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the amount of $60 million. Borrowings under the line of credit will bear interest at a rate of 10% per annum and may be repaid and reborrowed at any time. The credit agreement includes various customary remedies for the lender following an event of default, including the acceleration of repayment of outstanding amounts under line of credit. The line of credit matures on November 8, 2023.

On February 1, 2019, we borrowed $28.8 million under the line of credit; no amounts were previously outstanding under the line of credit. We intend to use the proceeds of the $28.8 million borrowing to repurchase the 2033 Senior Notes (as defined below) tendered by holders thereof pursuant to such holders option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes. We intend to use a portion of the proceeds of this offering to repay the $28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit and to terminate the line of credit thereafter.

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SELECTED FINANCIAL DATA

The following selected historical consolidated statement of operations data for the years ended December 31, 2017, 2016, 2015, 2014 and 2013 and the consolidated balance sheet data as of December 31, 2017, 2016, 2015, 2014 and 2013, below are derived from our audited consolidated financial statements and related notes thereto. The following selected historical consolidated statement of operations data for the period January 1, 2018 through September 30, 2018, and the consolidated balance sheet data as of September 30, 2018, are derived from our unaudited condensed consolidated financial statements and related notes thereto. This data should be read in conjunction with our Management s Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and the related notes contained in our Form 8-K filed with the SEC on January 28, 2019 and our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2018.

Effective January 1, 2018, we adopted Accounting Standards Codification Topic 606, Revenue from Contracts with Customers, using the full retrospective transition method. The information contained in the table below for the nine months ended September 30, 2017, and the years ended December 31, 2017, 2016 and 2015 has been adjusted to reflect our retrospective adoption of Topic 606. The information for the years ended December 31, 2014 and 2013 has not been adjusted to reflect the impact of the adoption of ASC 606.

(In thousands, except share and per share information)	For the periods January 1 through September 30,		For the years ended December 31,				
	2018	2017	2017	2016	2015	2014	2013
Statement of operations data:							
Revenues	$ 768,412	$ 805,022	$ 966,006	$ 1,117,494	$ 447,517	$ 91,125	$ 96,530
Costs and expenses:							
Cost of revenue	455,105	463,511	620,130	611,482	235,239	48,009	48,860
Operating expenses	394,491	460,322	622,318	602,563	332,858	188,931	127,302
Total costs and expenses	849,596	923,833	1,242,448	1,214,045	568,097	236,940	176,162
Operating loss	(81,184)	(118,811)	(276,442)	(96,551)	(120,580)	(145,815)	(79,632)
Other income and (expense), net	5,320	937	4,518	(271)	(39,517)	(25,212)	(24,586)

Income tax benefit (provision)	10,437	42,309	(18,855)	56,115	113,675	(24)	(1,672)
Net loss	(76,969)	(87,336)	(305,250)	(48,359)	(53,527)	(174,638)	(117,346)
Net loss attributable to common shareholders	$ (76,969)	$ (87,336)	$ (305,250)	$ (48,359)	$ (52,127)	$ (171,666)	$ (114,827)
Loss per share, basic and undiluted:							
Net loss per share, basic	$ (0.14)	$ (0.16)	$ (0.55)	$ (0.09)	$ (0.11)	$ (0.41)	$ (0.32)
Net loss per share, diluted	$ (0.14)	$ (0.16)	$ (0.55)	$ (0.10)	$ (0.11)	$ (0.41)	$ (0.32)
Weighted average number of common shares outstanding basic:	559,601,097	559,065,232	559,160,565	550,846,553	488,065,908	422,014,039	355,095,701
Weighted average number of common shares outstanding diluted:	559,601,097	559,065,232	559,160,565	555,605,448	488,065,908	422,014,039	355,095,701
Balance sheet data:							
Total assets	$ 2,480,994	$ 2,721,990	$ 2,589,956	$ 2,766,619	$ 2,799,188	$ 1,267,664	$ 1,391,516
Long-term liabilities	$ 374,521	$ 390,008	$ 434,304	$ 480,166	$ 614,423	$ 348,812	$ 426,687
Total shareholders equity	$ 1,788,643	$ 2,057,882	$ 1,843,623	$ 2,046,433	$ 1,957,695	$ 835,741	$ 872,979

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DESCRIPTION OF NOTES

We will issue the 4.50% Convertible Senior Notes due 2025 (the notes) under a base indenture (the base indenture) to be dated as of February 7, 2019, the date of initial issuance of the notes, between us and U.S. Bank, National Association, as trustee (the trustee), as supplemented by a supplemental indenture (the supplemental indenture), to be dated as of February 7, 2019, with respect to the notes. In this section, and throughout this prospectus supplement, we refer to the base indenture, as supplemented by the supplemental indenture, as the indenture. This description of notes supplements the description of the general provisions of the notes and the base indenture in the accompanying prospectus. The terms of the notes include those expressly set forth in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as amended (the Trust Indenture Act).

The following description is a summary of the material provisions of the notes and the indenture and does not purport to be complete. This summary is subject to and is qualified by reference to all of the provisions of the notes and the indenture, including the definitions of certain terms used in the indenture. We urge you to read these documents because they, and not this description, define your rights as a holder of the notes.

You may request a copy of the indenture from us as described under Where You Can Find More Information.

For purposes of this description, references to OPKO, the Company, we, our and us refer only to OPKO Health, and not to our subsidiaries, unless the context otherwise requires.

General

The notes will:

- be our general unsecured, senior obligations;
- initially be limited to an aggregate principal amount of $200.0 million (or $230.0 million if the underwriter s overallotment option to purchase additional notes is exercised in full);
- bear cash interest from February 7, 2019 at an annual rate of 4.50%, payable semiannually on February 15 and August 15 of each year, beginning on August 15, 2019;
- be subject to redemption at our option, on or after February 15, 2022, if the last reported sale price of our common stock has been at least 130% of the conversion price for the notes then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date;
- be subject to repurchase by us at the option of the holders following a fundamental change (as defined below under Fundamental Change Permits Holders to Require Us to Repurchase Notes) at

a repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date;

mature on February 15, 2025, unless earlier converted, redeemed or repurchased;

be issued in denominations of $1,000 and integral multiples of $1,000; and

be represented by one or more registered notes in global form, but in certain limited circumstances may be represented by notes in definitive form. See Book-Entry, Settlement and Clearance.

Subject to satisfaction of certain conditions and during the periods described below, the notes may be converted at an initial conversion rate of 236.7424 shares of common stock per $1,000 principal amount of notes

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(equivalent to an initial conversion price of approximately $4.22 per share of common stock). The conversion rate is subject to adjustment if certain events occur.

We will settle conversions of notes by paying or delivering, as the case may be, cash, shares of our common stock, or a combination of cash and shares of our common stock, at our election, as described under Conversion Rights Settlement upon Conversion. You will not receive any separate cash payment for interest, if any, accrued and unpaid to the conversion date except under the limited circumstances described below.

The indenture does not limit the amount of debt that may be issued by us or our subsidiaries under the indenture or otherwise. The indenture does not contain any financial covenants and does not restrict us from paying dividends or issuing or repurchasing our other securities. Other than restrictions described under Fundamental Change Permits Holders to Require Us to Repurchase Notes and Consolidation, Merger or Sale of Assets below and except for the provisions set forth under Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption, the indenture does not contain any covenants or other provisions designed to afford holders of the notes protection in the event of a highly leveraged transaction involving us or in the event of a decline in our credit rating as the result of a takeover, recapitalization, highly leveraged transaction or similar restructuring involving us that could adversely affect such holders.

We may, without the consent of the holders, reopen the indenture for the notes and issue additional notes under the indenture with the same terms as the notes offered hereby (other than differences in the issue price and interest accrued prior to the issue date of such additional notes) in an unlimited aggregate principal amount; *provided* that if any such additional notes are not fungible with the notes initially offered hereby for U.S. federal income tax or securities law purposes, such additional notes will have one or more separate CUSIP numbers.

We do not intend to list the notes on any securities exchange or any automated dealer quotation system.

References in this prospectus supplement to a holder or holders of notes that are held through DTC are references to owners of beneficial interests in such notes, unless the context otherwise requires. However, we and the trustee will treat the person in whose name the notes are registered (Cede & Co., in the case of notes held through DTC) as the owner of such notes for all purposes. References herein to the close of business refer to 5:00 p.m., New York City time, and to the open of business refer to 9:00 a.m., New York City time.

Purchase and Cancellation

The registrar, paying agent and conversion agent (if other than the trustee) will forward to the trustee all notes surrendered for payment, repurchase (including as described below), redemption, registration of transfer or exchange or conversion. All notes delivered to the trustee shall be cancelled promptly by the trustee. Except for any notes surrendered for registration of transfer or exchange, no notes shall be authenticated in exchange for any notes cancelled as provided in the indenture.

We may, to the extent permitted by law, and without the consent of holders, directly or indirectly (regardless of whether such notes are surrendered to us), repurchase notes in the open market or otherwise, whether by us or our subsidiaries or through a private or public tender or exchange offer or through counterparties to private agreements, including by cash-settled swaps or other derivatives. We will cause any notes so repurchased (other than notes repurchased pursuant to cash-settled swaps or other derivatives) to be surrendered to the trustee for cancellation, and they will no longer be considered outstanding under the indenture upon their repurchase.

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Payments on the Notes; Paying Agent and Registrar; Transfer and Exchange

We will pay or cause the paying agent to pay the principal of, and interest on, notes in global form registered in the name of or held by DTC or its nominee by wire transfer in immediately available funds to DTC or its nominee, as the case may be, as the registered holder of such global note.

We will pay or cause the paying agent to pay the principal of any certificated notes at the office or agency designated by us for that purpose. We have initially designated the trustee as our paying agent and registrar and its agency in the continental United States as a place where notes may be presented for payment or for registration of transfer. We may, however, change the paying agent or registrar without prior notice to the holders of the notes, and we may act as paying agent or registrar. Interest on certificated notes will be payable (i) to holders having an aggregate principal amount of $1,000,000 or less, by check mailed to the holders of these notes and (ii) to holders having an aggregate principal amount of more than $1,000,000, either by check mailed to each holder or, upon application by such a holder to the registrar not later than the relevant regular record date, by wire transfer in immediately available funds to that holder s account within the United States if such holder has provided us, the trustee or the paying agent (if other than the trustee) with the requisite information necessary to make such wire transfer, which application shall remain in effect until the holder notifies, in writing, the registrar of the notes to the contrary.

A holder of notes may transfer or exchange notes at the office of the registrar in accordance with the indenture. The registrar and the trustee may require a holder, among other things, to furnish appropriate endorsements and transfer documents. No service charge will be imposed by us, the trustee or the registrar for any registration of transfer or exchange of notes, but we may require a holder to pay a sum sufficient to cover any transfer tax or other similar governmental charge required by law or permitted by the indenture. We are not required to transfer or exchange any note selected for redemption or surrendered for conversion or required repurchase.

The registered holder of a note will be treated as its owner for all purposes.

Interest

The notes will bear cash interest at a rate of 4.50% per year until maturity of the notes. Interest on the notes will accrue from February 7, 2019 or from the most recent date on which interest has been paid or duly provided for. Interest will be payable semiannually in arrears on February 15 and August 15 of each year, beginning on August 15, 2019.

Interest will be paid to the person in whose name a note is registered at the close of business on February 1 or August 1, as the case may be, immediately preceding the relevant interest payment date (each, a regular record date). Interest on the notes will be computed on the basis of a 360-day year composed of twelve 30-day months, and, for partial months, on the basis of the number of days actually elapsed in a 30-day month.

If any interest payment date, the maturity date or any earlier required repurchase date upon a fundamental change repurchase date of a note falls on a day that is not a business day, the required payment will be made on the next succeeding business day and no interest on such payment will accrue in respect of the delay. The term business day means, with respect to any note, any day other than a Saturday, a Sunday or a day on which the Federal Reserve Bank of New York is authorized or required by law or executive order to close or be closed.

Unless the context otherwise requires, all references to interest in this prospectus supplement include additional interest, if any, payable at our election as the sole remedy relating to the failure to comply with our reporting obligations as described under Events of Default.

Ranking

The notes will be our senior unsecured obligations that rank senior in right of payment to all of our indebtedness that is expressly subordinated in right of payment to the notes. The notes will rank equal in right of

payment to all of our unsecured indebtedness that is not so subordinated. The notes will effectively rank junior to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness. The notes will be structurally junior to all existing and future indebtedness and other liabilities of our current or future subsidiaries (including trade payables). In the event of our bankruptcy, liquidation, reorganization or other winding up, our assets that secure secured debt will be available to pay obligations on the notes only after all indebtedness under such secured debt has been repaid in full from such assets. We advise you that there may not be sufficient assets remaining to pay amounts due on any or all the notes then outstanding.

As of September 30, 2018, we had $205.6 million of outstanding indebtedness for borrowed money (excluding intercompany debt) and our subsidiaries had $486.8 million of indebtedness and other liabilities (including trade payables but excluding intercompany obligations and liabilities of a type not required to be reflected on a balance sheet of such subsidiaries in accordance with U.S. GAAP) to which the notes would have been structurally subordinated. After giving effect to the issuance of the notes (assuming no exercise of the underwriter s overallotment option to purchase additional notes, our and our subsidiaries total indebtedness for borrowed money as of September 30, 2018 (excluding intercompany debt) would have been $405.6 million.

A substantial portion of our operations is conducted through our subsidiaries. The notes will not be guaranteed by any of our current or future subsidiaries. Our subsidiaries are separate and distinct legal entities and have no obligation, contingent or otherwise, to pay amounts due with respect to the notes or to make any funds available therefor, whether by dividends, loans or other payments. Our right to receive any assets of any of our subsidiaries upon such subsidiary s bankruptcy, liquidation or reorganization, and, therefore, the rights of the holders of notes to participate in those assets, will be subject to prior claims of creditors of the subsidiary, including trade creditors, and such subsidiary may not have sufficient assets remaining to make any payments to us as a stockholder or otherwise. The ability of our subsidiaries to pay dividends and make other payments to us is restricted by, among other things, applicable corporate and other laws and regulations and may be restricted by agreements to which our subsidiaries may become a party.

We may not be able to pay the cash portions of any settlement amount upon conversion of the notes, or to pay cash for the fundamental change repurchase price upon a fundamental change if a holder requires us to repurchase notes as described below. See Risk Factors Additional Risks Related to this Offering and the Notes We may not have the ability to raise the funds necessary to settle conversions of the notes or to repurchase the notes upon a fundamental change, and our future debt may contain limitations on our ability to repurchase the notes.

Optional Redemption

No sinking fund is provided for the notes, which means that we are not required to redeem or retire the notes periodically. Prior to February 15, 2022, the notes will not be redeemable. On or after February 15, 2022, we may redeem for cash any or all of the notes, at our option, if the last reported sale price of our common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period (including the last trading day of such period) ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption. In the case of any optional redemption, we will provide not less than 30 scheduled trading days nor more than 60 calendar days notice before the redemption date to the trustee, the conversion agent (if other than the trustee), the paying agent (if other than the trustee) and each holder of notes, and the redemption price will be equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date (unless the redemption date falls after a regular record date but on or prior to the immediately succeeding interest payment date, in which case we will pay the full amount of accrued and unpaid interest to the holder of record as of the close of business on such regular record date, and the redemption price will be equal to 100% of the principal amount of the notes to be redeemed). The redemption date must be a business day. We may not specify a redemption date that falls on or after

the 26th scheduled trading day immediately preceding the maturity date.

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If less than all of the outstanding notes are to be redeemed, the trustee will select the notes to be redeemed in principal amounts of $1,000 or multiples of $1,000 by lot, pro rata or by another method the trustee in its discretion considers reasonable. If only a portion of a note is subject to redemption and that note is converted in part, then the converted portion of that note will be deemed to be from the portion of that note that was subject to redemption.

No notes may be optionally redeemed if the principal amount of the notes has been accelerated, and such acceleration has not been rescinded, on or prior to the redemption date (except in the case of an acceleration resulting from a default by us in the payment of the redemption price).

Conversion Rights

General

Prior to the close of business on the business day immediately preceding November 15, 2024, the notes will be convertible only upon satisfaction of one or more of the conditions described under the headings Conversion upon Satisfaction of Sale Price Condition, Conversion upon Satisfaction of Trading Price Condition, Conversion upon Notice of Redemption, and Conversion upon Specified Corporate Events. On or after November 15, 2024, until the close of business on the business day immediately preceding the maturity date, holders may convert all or any portion of their notes at the conversion rate at any time irrespective of the foregoing conditions.

The conversion rate for the notes will initially be 236.7424 shares of common stock per $1,000 principal amount of notes (equivalent to an initial conversion price of approximately $4.22 per share of common stock). Upon conversion of a note, we will satisfy our conversion obligation by paying or delivering, as the case may be, cash, shares of our common stock, or a combination of cash and shares of our common stock, at our election, all as set forth below under Settlement upon Conversion. If we satisfy our conversion obligation solely in cash or through payment and delivery, as the case may be, of a combination of cash and shares of our common stock, the amount of cash and shares of common stock, if any, due upon conversion will be based on a daily conversion value (as defined below) calculated on a proportionate basis for each trading day in a 25 trading-day observation period (as defined below under Settlement upon Conversion). The trustee will initially act as the conversion agent.

A holder may convert fewer than all of such holder s notes so long as the notes converted are a multiple of $1,000 principal amount.

If we call the notes for redemption, a holder of notes may convert all or any portion of such holder s notes only until the close of business on the scheduled trading day immediately preceding the redemption date, unless we fail to pay the redemption price (in which case a holder of notes may convert such holder s notes until the redemption price has been paid or duly provided for).

Upon conversion, you will not receive any separate cash payment for accrued and unpaid interest, if any, except as described below. We will not issue fractional shares of our common stock upon conversion of notes. Instead, we will pay cash in lieu of delivering any fractional share as described under Settlement upon Conversion. Our payment and delivery, as the case may be, to you of the cash, shares of our common stock, or a combination thereof, as the case may be, into which a note is convertible will be deemed to satisfy in full our obligation to pay:

the principal amount of the note; and

accrued and unpaid interest, if any, to, but not including, the relevant conversion date.

As a result, accrued and unpaid interest, if any, to, but not including, the relevant conversion date will be deemed to be paid in full rather than cancelled, extinguished or forfeited. Upon a conversion of notes into a

combination of cash and shares of our common stock, accrued and unpaid interest will be deemed to be paid first out of the cash paid upon such conversion.

Notwithstanding the immediately preceding paragraph, if notes are converted after 5:00 p.m., New York City time, on a regular record date for the payment of interest, holders of such notes at 5:00 p.m., New York City time, on such regular record date will receive the full amount of interest payable on such notes on the corresponding interest payment date notwithstanding the conversion. Notes surrendered for conversion during the period from 5:00 p.m., New York City time, on any regular record date to 9:00 a.m., New York City time, on the immediately following interest payment date must be accompanied by funds equal to the amount of interest payable on the notes so converted; *provided* that no such payment need be made:

- for conversions of notes following the regular record date immediately preceding the maturity date;
- if we have specified a redemption date that is after a regular record date and on or prior to the business day immediately following the corresponding interest payment date;
- if we have specified a fundamental change repurchase date that is after a regular record date and on or prior to the business day immediately following the corresponding interest payment date; or
- to the extent of any overdue interest, if any overdue interest exists at the time of conversion with respect to such note.

Therefore, for the avoidance of doubt, all record holders on the regular record date immediately preceding the maturity date, any fundamental change repurchase date or redemption date, in each case, described above, will receive the full interest payment due on the maturity date or other applicable interest payment date in cash, regardless of whether their notes have been converted following such regular record date.

If a holder converts notes, we will pay any documentary, stamp or similar issue or transfer tax due on any issuance of any shares of our common stock upon the conversion, unless the tax is due because the holder requests any such shares to be issued in a name other than the holder s name, in which case the holder will pay that tax.

Holders may surrender their notes for conversion only under the following circumstances:

Conversion upon Satisfaction of Sale Price Condition

Prior to the close of business on the business day immediately preceding November 15, 2024, a holder of notes may surrender all or a portion of its notes for conversion during any calendar quarter commencing after the calendar quarter ending on March 31, 2019 (and only during such calendar quarter), if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during the period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day.

The last reported sale price of our common stock (or other security for which a closing sale price must be determined) on any date means the closing sale price per share (or if no closing sale price is reported, the average of the bid and

ask prices or, if more than one in either case, the average of the average bid and the average ask prices) on that date as reported in composite transactions for the principal U.S. national or regional securities exchange on which our common stock (or such other security) is traded. If our common stock (or such other security) is not listed for trading on a U.S. national or regional securities exchange on the relevant date, the last reported sale price will be the last quoted bid price for our common stock (or such other security) in the over-the-counter market on the relevant date as reported by OTC Markets Group Inc. or a similar organization. If our common stock (or such other security) is not so quoted, the last reported sale price will be the average of the mid-point of the last bid and ask prices for our common stock (or such other security) on the relevant date from each of at least three nationally recognized independent investment banking firms selected by us for this purpose. The last reported sale price will be determined without regard to after-hours trading or any other trading outside of the regular trading session hours.

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Except for purposes of determining amounts due upon conversion, trading day means a day on which (i) trading in our common stock (or other security for which a closing sale price must be determined) generally occurs on the Nasdaq Global Select Market or, if our common stock (or such other security) is not then listed on the Nasdaq Global Select Market, on the principal other U.S. national or regional securities exchange on which our common stock (or such other security) is then listed or, if our common stock (or such other security) is not then listed on a U.S. national or regional securities exchange, on the principal other market on which our common stock (or such other security) is then traded and (ii) a last reported sale price for our common stock (or closing sale price for such other security) is available on such securities exchange or market. If our common stock (or such other security) is not so listed or traded, trading day means a business day.

Conversion upon Satisfaction of Trading Price Condition

Prior to the close of business on the business day immediately preceding November 15, 2024, a holder of notes may surrender all or any portion of its notes for conversion at any time during the five business-day period after any five consecutive trading-day period (the measurement period) in which the trading price per $1,000 principal amount of notes, as determined following a request by a holder of notes in accordance with the procedures described below, for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each such trading day (the trading price condition).

The trading price of the notes on any date of determination means the average of the secondary market bid quotations obtained by the bid solicitation agent for $2,000,000 principal amount of notes at approximately 3:30 p.m., New York City time, on such determination date from three independent nationally recognized securities dealers we select for this purpose; *provided* that if three such bids cannot reasonably be obtained by the bid solicitation agent but two such bids are obtained, then the average of the two bids shall be used, and if only one such bid can reasonably be obtained by the bid solicitation agent, that one bid shall be used. If, on any date, the bid solicitation agent cannot reasonably obtain at least one bid for $2,000,000 principal amount of notes on such date from a nationally recognized securities dealer, then the trading price per $1,000 principal amount of notes will be deemed to be less than 98% of the product of the last reported sale price of our common stock and the conversion rate. If (x) we are not acting as bid solicitation agent, and we do not, when we are required to, instruct the bid solicitation agent in writing to obtain bids, or if we give such written instruction to the bid solicitation agent, and the bid solicitation agent fails to make such determination, or (y) we are acting as bid solicitation agent and we fail to obtain such bids, then, in either case, the trading price per $1,000 principal amount of notes will be deemed to be less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each trading day of such failure.

The bid solicitation agent (if other than us) shall have no obligation to determine the trading price per $1,000 principal amount of notes unless we have requested such determination in writing; and we will have no obligation to make such request (or, if we are acting as bid solicitation agent, we shall have no obligation to determine the trading price) unless a holder provides us with reasonable evidence that the trading price per $1,000 principal amount of notes would be less than 98% of the product of the last reported sale price of our common stock and the conversion rate. At such time, we will (i) instruct the three independent nationally recognized securities dealers to deliver bids to the bid solicitation agent and (ii) instruct the bid solicitation agent (if other than us) to determine, or if we are acting as bid solicitation agent, we shall determine, the trading price per $1,000 principal amount of notes in each case, beginning on the next trading day and on each successive trading day until the trading price per $1,000 principal amount of notes is greater than or equal to 98% of the product of the last reported sale price of our common stock and the conversion rate. If the trading price condition has been met, we will so notify the holders, the trustee and the conversion agent (if other than the trustee) in writing. If, at any time after the trading price condition has been met, the trading price per $1,000 principal amount of notes is greater than or equal to 98% of the product of the last reported sale price of our common stock

and the conversion rate for such date, we will so notify the holders, the trustee and the conversion agent (if other than the trustee) in writing.

We will initially act as the bid solicitation agent.

Conversion upon Notice of Redemption

If we call the notes for redemption, holders may convert all or any portion of their notes at any time prior to the close of business on the scheduled trading day prior to the redemption date, even if the notes are not otherwise convertible at such time. After that time, the right to convert notes on account of our delivery of the notice of redemption will expire, unless we default in the payment of the redemption price, in which case a holder of notes may convert all or any portion of its notes until the close of business on the scheduled trading day immediately preceding the date on which the redemption price has been paid or duly provided for.

Conversion upon Specified Corporate Events

Certain Distributions

If, prior to the close of business on the business day immediately preceding November 15, 2024, we elect to:

issue to all or substantially all holders of our common stock any rights, options or warrants (other than in connection with a stockholder rights plan so long as such rights have not separated from the shares of common stock) entitling them, for a period of not more than 60 calendar days after the announcement date of such issuance, to subscribe for or purchase shares of our common stock at a price per share that is less than the average of the last reported sale prices of our common stock for the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the date of announcement of such issuance; or

distribute to all or substantially all holders of our common stock our assets, securities or rights to purchase our securities, which distribution has a per share value, as determined by our board of directors or a committee thereof, exceeding 10% of the last reported sale price of our common stock on the trading day preceding the date of announcement for such distribution,

then, in either case, we must notify the holders of the notes, the trustee and the conversion agent (if other than the trustee) in writing at least 30 scheduled trading days prior to the ex-dividend date (as defined below) for such issuance or distribution (or, if later in the case of any such separation of rights issued pursuant to a stockholder rights plan, as soon as reasonably practicable after we become aware that such separation or triggering event has occurred or will occur). Once we have given such notice, holders may surrender all or any portion of their notes for conversion at any time until the earlier of 5:00 p.m., New York City time, on the business day immediately preceding the ex-dividend date for such issuance or distribution and our announcement that such issuance or distribution will not take place (or in the case of a separation or triggering event, until the 20th trading day following the date of our notice), even if the notes are not otherwise convertible at such time.

Holders of the notes may not convert their notes pursuant to this provision if they participate, at the same time and upon the same terms as holders of our common stock and solely as a result of holding the notes, in any of the transactions described above without having to convert their notes as if they held a number of shares of common stock

equal to the conversion rate, multiplied by the principal amount (expressed in thousands) of notes held by such holder.

Certain Corporate Events

If (i) a transaction or event that constitutes (x) a fundamental change (as defined under Fundamental Change Permits Holders to Require Us to Repurchase Notes) or (y) a make-whole fundamental change (as

defined under Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption) occurs prior to the close of business on the business day immediately preceding November 15, 2024, regardless of whether a holder has the right to require us to repurchase the notes as described under Fundamental Change Permits Holders to Require Us to Repurchase Notes or (ii) we are a party to a share exchange event (as defined under Recapitalizations, Reclassifications and Changes of Our Common Stock) (other than a share exchange event that is solely for the purpose of changing our jurisdiction of organization that (x) does not constitute a fundamental change or a make-whole fundamental change and (y) results in a reclassification, conversion or exchange of outstanding shares of our common stock solely into shares of common stock of the surviving entity and such common stock becomes reference property for the notes) that occurs prior to the close of business on the business day immediately preceding November 15, 2024 (each such fundamental change, make-whole fundamental change or share exchange event, a corporate event), all or any portion of a holder s notes may be surrendered for conversion at any time after the effective date for such corporate event until the earlier of (x) 35 trading days after the actual effective date of such corporate event or, if such corporate event also constitutes a fundamental change, until the close of business on the business day immediately preceding the related fundamental change repurchase date and (y) the scheduled trading day immediately preceding the maturity date. We will notify holders, the trustee and the conversion agent (if other than the trustee) in writing within three business days following the date we publicly announce such corporate event but in no event later than the actual effective date of such corporate event.

Conversions during the Three Months Immediately Preceding the Maturity Date

On or after November 15, 2024, a holder may convert all or any portion of its notes at any time prior to the close of business on the business day immediately preceding the maturity date regardless of the foregoing conditions.

Conversion Procedures

If you hold a beneficial interest in a global note (as defined below), to convert you must comply with DTC s procedures for converting a beneficial interest in a global note and, if required, pay funds equal to interest payable on the next interest payment date to which you are not entitled.

If you hold a certificated note (as defined below), to convert you must:

- complete and manually sign the conversion notice on the back of the note, or a facsimile of the conversion notice;
- deliver the conversion notice, which is irrevocable, and the note to the conversion agent;
- if required, furnish appropriate endorsements and transfer documents; and
- if required, pay funds equal to interest payable on the next interest payment date to which you are not entitled.

We will pay any documentary, stamp or similar issue or transfer tax on the issuance of any shares of our common stock upon conversion of the notes, unless the tax is due because the holder requests such shares to be issued in a name other than the holder s name, in which case the holder will pay the tax.

We refer to the date you comply with the relevant procedures for conversion described above as the conversion date.

If a holder has already delivered a repurchase notice as described under Fundamental Change Permits Holders to Require Us to Repurchase Notes with respect to a note, the holder may not surrender that note for conversion until the holder has validly withdrawn the repurchase notice in accordance with the relevant provisions of the indenture. If a holder submits its notes for required repurchase, the holder s right to withdraw the repurchase notice and convert the notes that are subject to repurchase will terminate at the close of business on the business day immediately preceding the fundamental change repurchase date.

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Settlement upon Conversion

Upon conversion, we may choose to pay or deliver, as the case may be, either cash (cash settlement), shares of our common stock (physical settlement) or a combination of cash and shares of our common stock (combination settlement), as described below. We refer to each of these settlement methods as a settlement method.

All conversions for which the relevant conversion date occurs on or after November 15, 2024, and all conversions for which the conversion date occurs after our issuance of a notice of redemption and prior to the related redemption date, will be settled using the same settlement method. Except for any conversions that occur after our issuance of a notice of redemption, but prior to the related redemption date, and any conversions for which the relevant conversion date occurs on or after November 15, 2024, we will use the same settlement method for all conversions occurring on the same conversion date, but we will not have any obligation to use the same settlement method with respect to conversions that occur on different conversion dates. That is, we may choose for notes converted on one conversion date to settle conversions in physical settlement, and choose for notes converted on another conversion date cash settlement or combination settlement.

If we elect a settlement method, we will inform holders of the notes so converting, the trustee and the conversion agent (if other than the trustee) of the settlement method we have selected no later than the close of business on the trading day immediately following the related conversion date (or in the case of any conversions occurring (i) after the date of issuance of a notice of redemption as described under Optional Redemption and prior to the related redemption date, in such notice of redemption or (ii) on or after November 15, 2024, no later than the close of business on the scheduled trading day immediately preceding November 15, 2024). If we do not timely elect a settlement method, we will no longer have the right to elect cash settlement or physical settlement and we will be deemed to have elected combination settlement in respect of our conversion obligation, as described below, and the specified dollar amount (as defined below) per $1,000 principal amount of notes will be equal to $1,000. If we elect combination settlement, but we do not timely notify converting holders, the trustee and the conversion agent (if other than the trustee) in writing of the specified dollar amount per $1,000 principal amount of notes, such specified dollar amount will be deemed to be $1,000. It is our current intent to settle conversions through combination settlement with a specified dollar amount per $1,000 principal amount of notes of $1,000.

Settlement amounts will be computed as follows:

- if we elect physical settlement, we will deliver to the converting holder in respect of each $1,000 principal amount of notes being converted a number of shares of common stock equal to the conversion rate;

- if we elect cash settlement, we will pay to the converting holder in respect of each $1,000 principal amount of notes being converted cash in an amount equal to the sum of the daily conversion values for each of the 25 consecutive trading days during the related observation period; and

- if we elect (or are deemed to have elected) combination settlement, we will pay or deliver, as the case may be, to the converting holder in respect of each $1,000 principal amount of notes being converted a settlement amount equal to the sum of the daily settlement amounts for each of the 25 consecutive trading days during the related observation period.

If more than one note is surrendered for conversion at any one time by the same holder, the conversion obligation with respect to such notes shall be computed on the basis of the aggregate principal amount of the notes surrendered.

The daily settlement amount, for each of the 25 consecutive trading days during the observation period, will consist of:

cash equal to the lesser of (i) the maximum cash amount per $1,000 principal amount of notes to be received upon conversion as specified in the notice specifying our chosen settlement method (or

deemed specified as set forth above) (the specified dollar amount), if any, divided by 25 (such quotient the daily measurement value) and (ii) the daily conversion value; and

if the daily conversion value exceeds the daily measurement value, a number of shares equal to (i) the difference between the daily conversion value and the daily measurement value, divided by (ii) the daily VWAP for such trading day.

The daily conversion value means, for each of the 25 consecutive trading days during the observation period, 4.0% of the product of (1) the conversion rate on such trading day and (2) the daily VWAP on such trading day.

The daily VWAP means, for each of the 25 consecutive trading days during the relevant observation period, the per share volume-weighted average price as displayed under the heading Bloomberg VWAP on Bloomberg page OPK <equity> AQR (or its equivalent successor if such page is not available) in respect of the period from the scheduled open of trading until the scheduled close of trading of the primary trading session on such trading day (or if such volume-weighted average price is unavailable, the market value of one share of our common stock on such trading day reasonably determined, using a volume-weighted average method, by a nationally recognized independent investment banking firm retained for this purpose by us). The daily VWAP will be determined without regard to after-hours trading or any other trading outside of the regular trading session trading hours.

The observation period with respect to any note surrendered for conversion means:

subject to the immediately succeeding bullet, if the relevant conversion date occurs prior to November 15, 2024, the 25 consecutive trading-day period beginning on, and including, the second trading day immediately succeeding such conversion date;

if the relevant conversion date occurs on or after the date of our issuance of a notice of redemption with respect to the notes as described under Optional Redemption and prior to the relevant redemption date, the 25 consecutive trading days beginning on, and including, the 26th scheduled trading day immediately preceding such redemption date; and

subject to the immediately preceding bullet, if the relevant conversion date occurs on or after November 15, 2024, the 25 consecutive trading days beginning on, and including, the 26th scheduled trading day immediately preceding the maturity date.

For the purposes of determining amounts due upon conversion only, trading day means a day on which (i) there is no market disruption event (as defined below) and (ii) trading in our common stock generally occurs on the Nasdaq Global Select Market or, if our common stock is not then listed on the Nasdaq Global Select Market, on the principal other U.S. national or regional securities exchange on which our common stock is then listed or, if our common stock is not then listed on a U.S. national or regional securities exchange, on the principal other market on which our common stock is then listed or admitted for trading. If our common stock is not so listed or admitted for trading, trading day means a business day.

Scheduled trading day means a day that is scheduled to be a trading day on the principal U.S. national or regional securities exchange or market on which our common stock is listed or admitted for trading. If our common stock is not so listed or admitted for trading, scheduled trading day means a business day.

For the purposes of determining amounts due upon conversion, market disruption event means (i) a failure by the primary U.S. national or regional securities exchange or market on which our common stock is listed or admitted for trading to open for trading during its regular trading session or (ii) the occurrence or existence prior to 1:00 p.m., New York City time, on any scheduled trading day for our common stock for more than one half-hour period in the aggregate during regular trading hours of any suspension or limitation imposed on trading (by reason of movements in price exceeding limits permitted by the relevant stock exchange or otherwise) in our common stock or in any options contracts or future contracts relating to our common stock.

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Except as described under Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption and Recapitalizations, Reclassifications and Changes of Our Common Stock, we will deliver the consideration due in respect of conversion on the second business day immediately following the relevant conversion date, if we elect physical settlement (*provided* that, with respect to any conversion date occurring after November 15, 2024, settlement will occur on the maturity date), or on the second business day immediately following the last trading day of the relevant observation period, in the case of any other settlement method.

We will pay cash in lieu of delivering any fractional share of common stock issuable upon conversion based on the daily VWAP on the relevant conversion date (in the case of physical settlement) or based on the daily VWAP on the last trading day of the relevant observation period (in the case of combination settlement).

Each conversion will be deemed to have been effected as to any notes surrendered for conversion on the conversion date; *provided*, *however*, that the person in whose name any shares of our common stock shall be issuable upon such conversion will become the holder of record of such shares as of the close of business on the conversion date (in the case of physical settlement) or the last trading day of the relevant observation period (in the case of combination settlement).

Conversion Rate Adjustments

The conversion rate will be adjusted as described below, except that we will not make any adjustments to the conversion rate if holders of the notes participate (other than in the case of a share split or share combination or a tender or exchange offer), at the same time and upon the same terms as holders of our common stock and solely as a result of holding the notes, in any of the transactions described below without having to convert their notes as if they held a number of shares of common stock equal to the conversion rate, *multiplied by* the principal amount (expressed in thousands) of notes held by such holder.

(1) If we exclusively issue shares of our common stock as a dividend or distribution on shares of our common stock, or if we effect a share split or share combination, the conversion rate will be adjusted based on the following formula:

$$CR_1 = CR_0 \times \frac{OS_1}{OS_0}$$

where,

CR_0 = the conversion rate in effect immediately prior to the open of business on the ex-dividend date of such dividend or distribution, or immediately prior to the open of business on the effective date of such share split or share combination, as applicable;

CR_1 = the conversion rate in effect immediately after the open of business on such ex-dividend date or effective date;

OS_0 = the number of shares of our common stock outstanding immediately prior to the open of business on such ex-dividend date or effective date (before giving effect to any such dividend, distribution, split or combination); and

OS_1 =

the number of shares of our common stock outstanding immediately after giving effect to such dividend, distribution, share split or share combination.

Any adjustment made under this clause (1) shall become effective immediately after the open of business on the ex-dividend date for such dividend or distribution, or immediately after the open of business on the effective date for such share split or share combination, as applicable. If any dividend or distribution of the type described

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in this clause (1) is declared but not so paid or made, the conversion rate shall be immediately readjusted, effective as of the date our board of directors or a committee thereof determines not to pay such dividend or distribution, to the conversion rate that would then be in effect if such dividend or distribution had not been declared.

(2) If we issue to all or substantially all holders of our common stock any rights, options or warrants (other than in connection with a stockholder rights plan) entitling them, for a period of not more than 60 calendar days after the announcement date of such issuance, to subscribe for or purchase shares of our common stock at a price per share that is less than the average of the last reported sale prices of our common stock for the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the date of announcement of such issuance, the conversion rate will be increased based on the following formula:

$$CR_1 = CR_0 \times \frac{OS_0 + Y}{OS_0 + Z}$$

where,

CR_0 = the conversion rate in effect immediately prior to the open of business on the ex-dividend date for such issuance;

CR_1 = the conversion rate in effect immediately after the open of business on such ex-dividend date;

OS_0 = the number of shares of our common stock outstanding immediately prior to the open of business on such ex-dividend date;

Y = the total number of shares of our common stock issuable pursuant to such rights, options or warrants; and

Z = the number of shares of our common stock equal to the aggregate price payable to exercise such rights, options or warrants, *divided* by the average of the last reported sale prices of our common stock over the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the date of announcement of the issuance of such rights, options or warrants.

Any increase made under this clause (2) will be made successively whenever any such rights, options or warrants are issued and shall become effective immediately after the open of business on the ex-dividend date for such issuance. To the extent that shares of common stock are not delivered after the expiration of such rights, options or warrants, the conversion rate shall be decreased to the conversion rate that would then be in effect had the increase with respect to the issuance of such rights, options or warrants been made on the basis of delivery of only the number of shares of common stock actually delivered. If such rights, options or warrants are not so issued, the conversion rate shall be decreased to the conversion rate that would then be in effect if such ex-dividend date for such issuance had not occurred.

For the purpose of this clause (2) and for the purpose of the first bullet point under Conversion upon Specified Corporate Events Certain Distributions, in determining whether any rights, options or warrants entitle the holders to subscribe for or purchase shares of our common stock at less than such average of the last reported sale prices for the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the date of announcement of such issuance, and in determining the aggregate offering price of such shares of common stock, there shall be taken into account any consideration received by us for such rights, options or warrants and any amount payable on exercise or conversion thereof, the value of such consideration, if other than cash, to be determined by our board of directors or a committee thereof.

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(3) If we distribute shares of our capital stock, evidences of our indebtedness, other assets or property of ours or rights, options or warrants to acquire our capital stock or other securities, to all or substantially all holders of our common stock, excluding:

dividends, distributions or issuances (including share splits) as to which an adjustment was effected pursuant to clause (1) or (2) above;

dividends or distributions paid exclusively in cash as to which the provisions set forth in clause (4) below shall apply;

except as otherwise described below, rights issued pursuant to a stockholder rights plan of ours;

distributions of reference property in a transaction described in Recapitalizations, Reclassifications, and Changes of Our Common Stock; and

spin-offs as to which the provisions set forth below in this clause (3) shall apply;

then the conversion rate will be increased based on the following formula:

$$CR_1 = CR_0 \times \frac{SP_0}{SP_0 \quad FMV}$$

where,

CR^0 = the conversion rate in effect immediately prior to the open of business on the ex-dividend date for such distribution;

CR_1 = the conversion rate in effect immediately after the open of business on such ex-dividend date;

SP_0 = the average of the last reported sale prices of our common stock over the 10 consecutive trading-day period ending on, and including, the trading day immediately preceding the ex-dividend date for such distribution; and

FMV = the fair market value (as determined by our board of directors or a committee thereof) of the shares of capital stock, evidences of indebtedness, assets, property, rights, options or warrants distributed with respect to each outstanding share of our common stock on the ex-dividend date for such distribution.

Any increase made under the portion of this clause (3) above will become effective immediately after the open of business on the ex-dividend date for such distribution. If such distribution is not so paid or made, the conversion rate shall be decreased to be the conversion rate that would then be in effect if such distribution had not been declared. If we issue rights, options or warrants that are only exercisable upon the occurrence of certain triggering events, then we will not adjust the conversion rate pursuant to the clauses above until the earliest of these triggering events occurs, and

we will readjust the conversion rate to the extent that any of these rights, options or warrants are not exercised before they expire. In the case of any distribution of rights, options or warrants, to the extent any such rights, options or warrants expire unexercised, the conversion rate shall be immediately readjusted to the conversion rate that would then be in effect had the increase made for the distribution of such rights, options or warrants been made on the basis of delivery of only the number of shares of our common stock actually delivered upon exercise of such rights, options or warrants.

Notwithstanding the foregoing, if FMV (as defined above) is equal to or greater than SP_0 (as defined above), in lieu of the foregoing increase, each holder of a note shall receive, in respect of each $1,000 principal amount thereof, at the same time and upon the same terms as holders of our common stock, the amount and kind of our capital stock, evidences of our indebtedness, other assets or property of ours or rights, options or warrants to acquire our capital stock or other securities that such holder would have received if such holder owned a number of shares of common stock equal to the conversion rate in effect on the ex-dividend date for the distribution.

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With respect to an adjustment pursuant to this clause (3) where there has been a payment of a dividend or other distribution on our common stock of shares of capital stock of any class or series, or similar equity interest, of or relating to a subsidiary or other business unit, that are, or, when issued, will be, listed or admitted for trading on a U.S. national securities exchange, which we refer to as a spin-off, the conversion rate will be increased based on the following formula:

$$CR_1 = CR_0 \times \frac{FMV_0 + MP_0}{MP_0}$$

where,

CR_0 = the conversion rate in effect immediately prior to the end of the valuation period (as defined below);

CR_1 = the conversion rate in effect immediately after the end of the valuation period;

FMV_0 = the average of the last reported sale prices of the capital stock or similar equity interest distributed to holders of our common stock applicable to one share of our common stock (determined by reference to the definition of last reported sale price set forth under Conversion upon Satisfaction of Sale Price Condition as if references therein to our common stock were to such capital stock or similar equity interest) over the first 10 consecutive trading day period after, and including, the ex-dividend date of the spin-off (the valuation period); *provided* that if there is no last reported sale price of the capital stock or similar equity interest distributed to the holders of our common stock on such ex-dividend date, the valuation period shall be the first ten consecutive trading day period after, and including, the first date such last reported sale price is available; and

MP_0 = the average of the last reported sale prices of our common stock over the valuation period.

The increase to the conversion rate under the preceding paragraph will occur at the close of business on the last trading day of the valuation period; provided that (x) in respect of any conversion of notes for which physical settlement is applicable, if the relevant conversion date occurs during the valuation period, the reference to 10 in the preceding paragraph shall be deemed replaced with such lesser number of trading days as have elapsed from, and including, the ex-dividend date for such spin-off to, and including, such conversion date in determining the conversion rate and (y) in respect of any conversion of notes for which cash settlement or combination settlement is applicable, for any trading day that falls within the relevant observation period for such conversion and within the valuation period, the reference to 10 in the preceding paragraph shall be deemed replaced with such lesser number of trading days as have elapsed from, and including, the ex-dividend date for such spin-off to, and including, such trading day in determining the conversion rate as of such trading day of such observation period. If any dividend or distribution that constitutes a spin-off is declared but not so paid or made, the conversion rate shall be immediately decreased, effective as of the date our board of directors or a committee thereof determines not to pay or make such dividend or distribution, to the conversion rate that would then be in effect if such dividend or distribution had not been declared or announced.

(4) If any cash dividend or distribution is made to all or substantially all holders of our common stock, the conversion rate will be adjusted based on the following formula:

$$CR_1 = CR_0 \times \frac{SP_0}{SP_0 \quad C}$$

where,

CR_0 = the conversion rate in effect immediately prior to the open of business on the ex-dividend date for such dividend or distribution;

CR_1 = the conversion rate in effect immediately after the open of business on the ex-dividend date for such dividend or distribution;

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SP_0 = the last reported sale price of our common stock on the trading day immediately preceding the ex-dividend date for such dividend or distribution; and

C = the amount in cash per share we distribute to all or substantially all holders of our common stock.

Any increase made under this clause (4) shall become effective immediately after the open of business on the ex-dividend date for such dividend or distribution. If such dividend or distribution is not so paid, the conversion rate shall be decreased, effective as of the date our board of directors or a committee thereof determines not to make or pay such dividend or distribution, to be the conversion rate that would then be in effect if such dividend or distribution had not been declared.

Notwithstanding the foregoing, if C (as defined above) is equal to or greater than SP_0 (as defined above), in lieu of the foregoing increase, each holder of a note shall receive, for each $1,000 principal amount of notes, at the same time and upon the same terms as holders of shares of our common stock, the amount of cash that such holder would have received if such holder owned a number of shares of our common stock equal to the conversion rate in effect on the ex-dividend date for such cash dividend or distribution.

(5) If we or any of our subsidiaries make a payment in respect of a tender or exchange offer for our common stock that is subject to the then-applicable tender offer rules under the Exchange Act, other than an odd lot tender offer, to the extent that the cash and value of any other consideration included in the payment per share of common stock exceeds the average of the last reported sale prices of our common stock over the 10 consecutive trading day period commencing on, and including, the trading day next succeeding the last date on which tenders or exchanges may be made pursuant to such tender or exchange offer, the conversion rate will be increased based on the following formula:

$$CR_1 = CR_0 \times \frac{AC + (SP_1 \times OS_1)}{OS \times SP_1}$$

where,

CR_0 = the conversion rate in effect immediately prior to the close of business on the 10th trading day immediately following, and including, the trading day next succeeding the date such tender or exchange offer expires;

CR_1 = the conversion rate in effect immediately after the close of business on the 10th trading day immediately following, and including, the trading day next succeeding the date such tender or exchange offer expires;

AC = the aggregate value of all cash and any other consideration (as determined by our board of directors or a committee thereof) paid or payable for shares purchased in such tender or exchange offer;

OS_0 = the number of shares of our common stock outstanding immediately prior to the date such tender or exchange offer expires (prior to giving effect to the purchase of all shares accepted for purchase or exchange in such tender or exchange offer);

OS_1 = the number of shares of our common stock outstanding immediately after the date such tender or exchange offer expires (after giving effect to the purchase of all shares accepted for purchase or exchange in such tender or exchange offer); and

SP_1 = the average of the last reported sale prices of our common stock over the 10 consecutive trading day period commencing on, and including, the trading day next succeeding the date such tender or exchange offer

expires.

The increase to the conversion rate under the preceding paragraph will occur at the close of business on the 10th trading day immediately following, and including, the trading day immediately following the date such

tender or exchange offer expires; provided that (x) in respect of any conversion of notes for which physical settlement is applicable, if the relevant conversion date occurs during the 10 trading days immediately following, and including, the trading day next succeeding the expiration date of any tender or exchange offer, references to 10 or 10th in the preceding paragraph shall be deemed replaced with such lesser number of trading days as have elapsed from, and including, the trading day next succeeding the expiration date of such tender or exchange offer to, and including, such conversion date in determining the conversion rate and (y) in respect of any conversion of notes for which cash settlement or combination settlement is applicable, for any trading day that falls within the relevant observation period for such conversion and within the 10 trading days immediately following, and including, the trading day immediately following the expiration date of any tender or exchange offer, references to 10 or 10th in the preceding paragraph shall be deemed replaced with such lesser number of trading days as have elapsed from, and including, the trading day next succeeding such expiration date of such tender or exchange offer to, and including, such trading day in determining the conversion rate as of such trading day.

If we are or one of our subsidiaries is obligated to purchase our common stock pursuant to any such tender or exchange offer described in this clause (5) but we are, or such subsidiary is, permanently prevented by applicable law from effecting any such purchase or all such purchases are rescinded, the conversion rate will be decreased to be the conversion rate that would then be in effect if such tender or exchange offer had not been made or had been made only in respect of the purchases that have been effected.

Notwithstanding the foregoing, if a conversion rate adjustment becomes effective on any ex-dividend date as described above, and a holder that has converted its notes on or after such ex-dividend date and on or prior to the related record date would be treated as the record holder of shares of our common stock as of the related conversion date as described under Settlement upon Conversion based on an adjusted conversion rate for such ex-dividend date, then, notwithstanding the foregoing conversion rate adjustment provisions, the conversion rate adjustment relating to such ex-dividend date will not be made for such converting holder. Instead, such holder will be treated as if such holder were the record owner of the shares of our common stock on an unadjusted basis and participate in the related dividend, distribution or other event giving rise to such adjustment.

Except as stated herein, we will not adjust the conversion rate for the issuance of shares of our common stock or any securities convertible into or exchangeable for shares of our common stock or the right to purchase shares of our common stock or such convertible or exchangeable securities.

As used in this section, ex-dividend date means the first date on which the shares of our common stock trade on the applicable exchange or in the applicable market, regular way, without the right to receive the issuance, dividend or distribution in question, from us or, if applicable, from the seller of our common stock on such exchange or market (in the form of due bills or otherwise) as determined by such exchange or market, and effective date means the first date on which the shares of our common stock trade on the applicable exchange or in the applicable market, regular way, reflecting the relevant share split or share combination, as applicable. For the avoidance of doubt, any alternative trading convention on the applicable exchange or market in respect of shares of our common stock under a separate ticker symbol or CUSIP number will not be considered regular way for this purpose.

As used in this section, record date means, with respect to any dividend, distribution or other transaction or event in which the holders of our common stock (or other applicable security) have the right to receive any cash, securities or other property or in which our common stock (or such other security) is exchanged for or converted into any combination of cash, securities or other property, the date fixed for determination of holders of our common stock (or such other security) entitled to receive such cash, securities or other property (whether such date is fixed by our board of directors or a duly authorized committee thereof, statute, contract or otherwise).

Subject to the applicable listing standards of the Nasdaq Global Select Market or the principal U.S. national or regional securities exchange on which our common stock is then traded if not the Nasdaq Global Select

Market, we are permitted to increase the conversion rate of the notes by any amount for a period of at least 20 business days if our board of directors or a committee thereof determines that such increase would be in our best interest. Subject to the applicable listing standards of the Nasdaq Global Select Market or the principal U.S. national or regional securities exchange on which our common stock is then traded if not the Nasdaq Global Select Market, we may also (but are not required to) increase the conversion rate to avoid or diminish income tax to holders of our common stock or rights to purchase shares of our common stock in connection with a dividend or distribution of shares (or rights to acquire shares) or similar event.

A holder may, in some circumstances, including a distribution of cash dividends to holders of shares of our common stock, be deemed to have received a distribution subject to U.S. federal income tax as a result of an adjustment or the nonoccurrence of an adjustment to the conversion rate. For a discussion of the U.S. federal income tax treatment of an adjustment to the conversion rate, see U.S. Federal Income Tax Considerations.

If we have a rights plan in effect upon conversion of the notes into common stock, you will receive, in addition to any shares of common stock received in connection with such conversion, the rights under the rights plan. However, if, prior to any conversion, the rights have separated from the shares of common stock in accordance with the provisions of the applicable rights plan, the conversion rate will be adjusted at the time of separation as if we distributed to all or substantially all holders of our common stock, shares of our capital stock, evidences of indebtedness, assets, property, rights, options or warrants as described in clause (3) above, subject to readjustment in the event of the expiration, termination or redemption of such rights.

Notwithstanding any of the foregoing, the conversion rate will not be adjusted:

upon the issuance of any shares of our common stock pursuant to any present or future plan providing for the reinvestment of dividends or interest payable on our securities and the investment of additional optional amounts in shares of our common stock under any plan;

upon the issuance of any shares of our common stock or options or rights to purchase those shares pursuant to any present or future employee, director or consultant benefit or incentive plan or program of or assumed by us or any of our subsidiaries;

upon the issuance of any shares of our common stock pursuant to any option, warrant, right or exercisable, exchangeable or convertible security not described in the preceding bullet and outstanding as of the date the notes were first issued;

upon the repurchase of any shares of our common stock pursuant to an open-market share repurchase program or other buy-back transaction (including, without limitation, through any structured or derivative transactions such as accelerated share repurchase transactions or similar forward derivatives), or other buy-back transaction, that is not a tender offer or exchange offer of the nature described under clause (5) above;

solely for a change in the par value (or lack of par value) of our common stock; or

for accrued and unpaid interest, if any.

We will not adjust the conversion rate pursuant to the clauses above unless the adjustment would result in a change of at least 1% in the then effective conversion rate. However, we will carry forward any adjustment to the conversion rate that we would otherwise have to make and take that adjustment into account in any subsequent adjustment. Notwithstanding the foregoing, all such carried-forward adjustments shall be made with respect to the notes (i) in connection with any subsequent adjustment to the conversion rate of at least 1% of the conversion rate, (ii) regardless of whether the aggregate adjustment is less than 1% of the conversion rate, (x) on the conversion date (in the case of physical settlement) or (y) on each trading day of any observation period (in the case of cash settlement or combination settlement) and (iii) on the effective date of any make-whole fundamental change, in each case, unless the adjustment has already been made. Adjustments to the conversion rate will be calculated to the nearest 1/10,000th of a share.

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Recapitalizations, Reclassifications and Changes of Our Common Stock

In the case of:

- any recapitalization, reclassification or change of our common stock (other than changes resulting from a subdivision or combination),
- any consolidation, merger or combination involving us,
- any sale, lease or other transfer to a third party of the consolidated assets of ours and our subsidiaries substantially as an entirety, or
- any statutory share exchange,

in each case, as a result of which our common stock would be converted into, or exchanged for, stock, other securities, other property or assets (including cash or any combination thereof) (any such event, a share exchange event), then we or the successor or purchasing company, as the case may be, will execute with the trustee and without the consent of the holders a supplemental indenture providing that at and after the effective time of the share exchange event, the right to convert each $1,000 principal amount of notes will be changed into a right to convert such principal amount of notes into the kind and amount of shares of stock, other securities or other property or assets (including cash or any combination thereof) that a holder of a number of shares of common stock equal to the conversion rate immediately prior to such share exchange event would have owned or been entitled to receive (the reference property) upon such share exchange event. The supplemental indenture providing that the notes will be convertible into reference property will provide for anti-dilution and other adjustments that are as nearly equivalent as possible to the adjustments described under Conversion Rate Adjustments above. If the reference property in respect of any transaction includes shares of stock, securities or other property or assets of a company other than us or the successor or purchasing corporation, as the case may be, in such transaction, such other company will also execute such supplemental indenture, and such supplemental indenture will contain such additional provisions to protect the interests of the holders, including the right of holders to require us to repurchase their notes upon a fundamental change as described under Fundamental Change Permits Holders to Require Us to Repurchase Notes below, as the board of directors reasonably considers necessary by reason of the foregoing. At and after the effective time of the share exchange event, (i) we will continue to have the right to determine the form of consideration to be paid or delivered, as the case may be, upon conversion of notes, as set forth under Settlement upon Conversion and (ii)(x) any amount payable in cash upon conversion of the notes as set forth under Settlement upon Conversion will continue to be payable in cash, (y) any shares of our common stock that we would have been required to deliver upon conversion of the notes as set forth under Settlement upon Conversion will instead be deliverable in the amount and type of reference property that a holder of that number of shares of our common stock would have received in such share exchange event and (z) the daily VWAP will be calculated based on the value of a unit of reference property that a holder of one share of our common stock would have received in such share exchange event. If the share exchange event causes our common stock to be converted into, or exchanged for, the right to receive more than a single type of consideration (determined based in part upon any form of stockholder election), the reference property into which the notes will be convertible will be deemed to be (i) the weighted average of the types and amounts of consideration received by the holders of our common stock that affirmatively make such an election or (ii) if no holders of our common stock affirmatively make such an election, the types and amount of consideration actually received by such holders. We will notify holders, the

trustee and the conversion agent (if other than the trustee) in writing of the weighted average as soon as practicable after such determination is made. If the holders of our common stock receive only cash in such share exchange event, then for all conversions that occur after the effective date of such share exchange event (i) the consideration due upon conversion of each $1,000 principal amount of notes shall be solely cash in an amount equal to the conversion rate in effect on the conversion date (as may be increased as described under Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption), multiplied by the price paid per share of common stock in such share exchange event and (ii) we will satisfy our conversion obligation by paying cash to converting holders on the second business day immediately following the conversion date.

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Adjustments of Prices

Whenever any provision of the indenture requires us to calculate the last reported sale prices, the daily VWAPs, the daily conversion values or the daily settlement amounts over a span of multiple days (including an observation period and the stock price for purposes of a make-whole fundamental change or redemption), we will make appropriate adjustments without duplication in respect of any adjustment made pursuant to the provisions described under Conversion Rate Adjustments above) to each to account for any adjustment to the conversion rate that becomes effective, or any event requiring an adjustment to the conversion rate where the ex-dividend date, effective date or expiration date of the event occurs, at any time during the period when such last reported sale prices, daily VWAPs, daily conversion values or daily settlement amounts are to be calculated.

Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption

If (i) the effective date (as defined below) of a fundamental change (as defined below and determined after giving effect to any exceptions to or exclusions from such definition, but without regard to subclause (a) of the proviso in clause (2) of the definition thereof, a make-whole fundamental change) occurs prior to the maturity date of the notes or (ii) we give a notice of optional redemption with respect to the notes as provided for under Optional Redemption and, in each case, a holder elects to convert its notes in connection with such make-whole fundamental change or redemption notice, as applicable, we will, under certain circumstances, increase the conversion rate for the notes so surrendered for conversion by a number of additional shares of common stock (the additional shares), as described below. A conversion of notes will be deemed for these purposes to be in connection with such make-whole fundamental change if the relevant notice of conversion of the notes is received by the conversion agent from, and including, the effective date of the make-whole fundamental change up to, and including, the business day immediately prior to the related fundamental change repurchase date (or, in the case of a make-whole fundamental change that would have been a fundamental change but for subclause (a) of the proviso in clause (2) of the definition thereof, the 30th trading day immediately following the effective date of such make-whole fundamental change). A conversion of notes will be deemed for these purposes to be in connection with a redemption notice if the notice of conversion of the notes is received by the conversion agent from, and including, the date of the redemption notice until the close of business on the business day immediately preceding the redemption date.

Upon surrender of notes for conversion in connection with a make-whole fundamental change or optional redemption, we will, at our option, satisfy our conversion obligation by physical settlement, cash settlement or combination settlement, based on the conversion rate as increased to reflect the additional shares pursuant to the table set forth below, as described under Settlement upon Conversion. However, if the consideration for our common stock in any make-whole fundamental change described in clause (2) of the definition of fundamental change is composed entirely of cash, for any conversion of notes following the effective date of such make-whole fundamental change, the conversion obligation will be calculated based solely on the stock price (as defined below) for the transaction and will be deemed to be an amount of cash per $1,000 principal amount of converted notes equal to the conversion rate (including any increase to reflect the additional shares as described in this section), *multiplied by* such stock price. In such event, the conversion obligation will be determined and paid to holders in cash on the second business day following the conversion date. We will notify holders, the trustee and the conversion agent (if other than the trustee) in writing of the effective date of any make-whole fundamental change no later than five business days after such effective date.

The number of additional shares, if any, by which the conversion rate will be increased will be determined by reference to the table below, based on the date on which the make-whole fundamental change occurs or becomes effective, or the date of the redemption notice, as the case may be (in each case, the effective date) and the price paid

(or deemed to be paid) per share of our common stock in the make-whole fundamental change or with respect to the optional redemption, as the case may be (the stock price). If the holders of our common stock receive in exchange for their common stock only cash in a make-whole fundamental change described in

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clause (2) of the definition of fundamental change, the stock price will be the cash amount paid per share. Otherwise, the stock price will be the average of the last reported sale prices of our common stock over the five trading-day period ending on, and including, the trading day immediately preceding the effective date of the make-whole fundamental change or the date of the redemption notice, as the case may be.

The stock prices set forth in the column headings of the table below will be adjusted as of any date on which the conversion rate of notes is otherwise adjusted. The adjusted stock prices will equal the stock prices immediately prior to such adjustment, *multiplied by* a fraction, the numerator of which is the conversion rate immediately prior to the adjustment giving rise to the stock price adjustment and the denominator of which is the conversion rate as so adjusted. The number of additional shares as set forth in the table below will be adjusted in the same manner and at the same time as the conversion rate as set forth under Conversion Rate Adjustments.

The following table sets forth the number of additional shares by which the conversion rate for the notes will be increased per $1,000 principal amount of notes for each stock price and effective date set forth below:

	Stock Price											
ffective ate	**$3.52**	**$4.00**	**$4.22**	**$4.75**	**$5.49**	**$6.50**	**$8.00**	**$10.00**	**$12.00**	**$15.00**	**$20.00**	**$25.00**
ebruary 7, 019	47.3485	47.3485	47.3485	47.3485	37.5692	27.0730	17.6326	10.6176	6.6409	3.3309	0.8926	0.0056
ebruary 15, 020	47.3485	47.3485	47.3485	46.4997	35.0015	24.8268	15.8576	9.3776	5.7826	2.8243	0.6926	0.0000
ebruary 15, 021	47.3485	47.3485	47.3485	42.8787	31.6142	21.9038	13.6451	7.8776	4.7659	2.2576	0.4826	0.0000
ebruary 15, 022	47.3485	47.3485	47.3485	37.9313	27.0615	18.1038	10.8576	6.0876	3.6076	1.6443	0.2876	0.0000
ebruary 15, 023	47.3485	47.3485	42.5426	31.0471	20.8698	13.1038	7.4326	4.0476	2.3659	1.0443	0.1126	0.0000
ebruary 15, 024	47.3485	38.5076	31.7708	20.6260	11.9828	6.5499	3.4701	1.9376	1.1659	0.5043	0.0026	0.0000
ebruary 15, 025	47.3485	13.2576	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

The exact stock prices and effective dates may not be set forth in the table above, in which case

If the stock price is between two stock prices in the table or the effective date is between two effective dates in the table, the number of additional shares by which the conversion rate for the notes will be increased will be determined by a straight-line interpolation between the number of additional shares set forth for the higher and lower stock prices and the earlier and later effective dates, as applicable, based on a 365-day year.

If the stock price is greater than $25.00 per share (subject to adjustment in the same manner as the stock prices set forth in the column headings of the table above), no additional shares will be added to the conversion rate for the notes.

If the stock price is less than $3.52 per share (subject to adjustment in the same manner as the stock prices set forth in the column headings of the table above), no additional shares will be added to the conversion rate for the notes.

Notwithstanding the foregoing, in no event will the conversion rate per $1,000 principal amount of notes exceed 284.0909 shares of common stock, subject to adjustment in the same manner as the conversion rate as set forth under Conversion Rate Adjustments.

Our obligation to increase the conversion rate for notes converted in connection with a make-whole fundamental change could be considered a penalty, in which case the enforceability thereof would be subject to general principles of reasonableness and equitable remedies.

Fundamental Change Permits Holders to Require Us to Repurchase Notes

If a fundamental change (as defined below in this section) occurs at any time prior to the maturity date of the notes, holders will have the right, at their option, to require us to repurchase for cash all of their notes, or any

portion of the principal thereof that is equal to $1,000 or a multiple of $1,000. The fundamental change repurchase date will be a date specified by us that is not less than 20 or more than 35 business days following the date of our fundamental change notice as described below.

The fundamental change repurchase price we are required to pay will be equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date (unless the fundamental change repurchase date falls after a regular record date but on or prior to the interest payment date to which such regular record date relates, in which case we will instead pay the full amount of accrued and unpaid interest to the holder of record on such regular record date, and the fundamental change repurchase price will be equal to 100% of the principal amount of the notes to be repurchased).

A fundamental change will be deemed to have occurred at the time after the notes are originally issued if any of the following occurs:

(1) a person or group within the meaning of Section 13(d) of the Exchange Act, other than us, our wholly-owned subsidiaries and our and their employee benefit plans and other than Phillip Frost, M.D. or entities directly or indirectly controlled by him or established for the benefit of him or his descendants or spouses or charities (collectively, the permitted owners), has become the direct or indirect beneficial owner, as defined in Rule 13d-3 under the Exchange Act, of our common equity representing more than 50% of the voting power of our common equity or the permitted owners have (or any group within the meaning of Section 13(d) of the Exchange Act including any permitted owner has) become the direct or indirect beneficial owners, as defined in Rule 13d-3 under the Exchange Act, of our common equity representing more than 70% of the voting power of our common equity;

(2) the consummation of (A) any recapitalization, reclassification or change of our common stock (other than changes resulting from a subdivision, a combination or merely a change in par value) as a result of which our common stock would be converted into, or exchanged for, stock, other securities, other property or assets; (B) any share exchange, consolidation or merger of us pursuant to which our common stock will be converted into cash, securities or other property or assets; or (C) any sale, lease or other transfer in one transaction or a series of related transactions of all or substantially all of the consolidated assets of us and our subsidiaries, taken as a whole, to any person other than one or more of our subsidiaries; *provided, however,* that neither (a) a transaction described in clause (B) in which the holders of all classes of our common equity immediately prior to such transaction own, directly or indirectly, more than 50% of all classes of common equity of the continuing or surviving corporation or transferee or the parent thereof immediately after such transaction in substantially the same proportions as such ownership immediately prior to such transaction or (b) any merger of us solely for the purpose of changing our jurisdiction of incorporation that results in a reclassification, conversion or exchange of outstanding shares of common stock solely into shares of common stock of the surviving entity shall be a fundamental change pursuant to this clause (2);

(3) our stockholders approve any plan or proposal for the liquidation or dissolution of us; or

(4) our common stock (or other common stock underlying the notes) ceases to be listed or quoted on any of the New York Stock Exchange, the Nasdaq Global Select Market or the Nasdaq Global Market (or any of their respective successors).

A transaction or transactions described in clause (2) above will not constitute a fundamental change, however, if at least 90% of the consideration received or to be received by our common stockholders, excluding cash payments for fractional shares or pursuant to statutory appraisal rights, in connection with such transaction or transactions consists of shares of common stock or other common equity that are listed or quoted on any of the New York Stock Exchange, the Nasdaq Global Select Market or the Nasdaq Global Market (or any of their respective successors) or will be so

listed or quoted when issued or exchanged in connection with such

transaction or transactions and as a result of such transaction or transactions the notes become convertible into such consideration, excluding cash payments for fractional shares or pursuant to statutory appraisal rights (subject to the provisions set forth above under Conversion Rights Settlement upon Conversion).

If any transaction in which our common stock is replaced by the securities of another entity occurs, following the effective date of such transaction, references to us in the definition of fundamental change above shall instead be references to such other entity.

For purposes of the definition of fundamental change above, any transaction that constitutes a fundamental change pursuant to both clause (1) and clause (2) of such definition (without giving effect to the proviso to clause (2)) shall be deemed a fundamental change solely under clause (2) of such definition (subject to the proviso to clause (2)).

Notwithstanding the foregoing, we will not be required to repurchase, or to make an offer to repurchase, the notes upon a fundamental change if a third party makes such an offer in the same manner, at the same time and otherwise in compliance with the requirements for an offer made by us as set forth above and such third party purchases all notes properly surrendered and not validly withdrawn under its offer in the same manner, at the same time and otherwise in compliance with the requirements for an offer made by us as set forth above.

On or before the 20th business day after the occurrence of a fundamental change, we will provide to all holders of the notes and the trustee and paying agent a written notice of the occurrence of the fundamental change and of the resulting repurchase right. Such notice shall state, among other things:

the events causing a fundamental change;

the effective date of the fundamental change;

the last date on which a holder may exercise the repurchase right;

the fundamental change repurchase price;

the fundamental change repurchase date;

the name and address of the paying agent and the conversion agent, if applicable;

if applicable, the conversion rate and any adjustments to the conversion rate;

that the notes with respect to which a fundamental change repurchase notice has been delivered by a holder may be converted only if the holder validly withdraws the fundamental change repurchase notice in accordance with the terms of the indenture; and

the procedures that holders must follow to require us to repurchase their notes.

To exercise the fundamental change repurchase right, you must deliver, on or before the close of business on the business day immediately preceding the fundamental change repurchase date, the notes to be repurchased, duly endorsed for transfer, together with a written repurchase notice, to the paying agent. Each repurchase notice must state:

if certificated, the certificate numbers of your notes to be delivered for repurchase or if not certificated, the notice must comply with applicable DTC procedures;

the portion of the principal amount of notes to be repurchased, which must be $1,000 or an integral multiple thereof; and

that the notes are to be repurchased by us pursuant to the applicable provisions of the notes and the indenture.

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Holders may withdraw any repurchase notice (in whole or in part) by a written notice of withdrawal delivered to the paying agent prior to the close of business on the business day immediately preceding the fundamental change repurchase date. The notice of withdrawal shall state:

- the principal amount of the withdrawn notes;
- if certificated notes have been issued, the certificate numbers of the withdrawn notes or, if not certificated, the notice must comply with applicable DTC procedures; and
- the principal amount, if any, which remains subject to the repurchase notice.

We will be required to repurchase the notes on the fundamental change repurchase date. Holders who have exercised the repurchase right will receive payment of the fundamental change repurchase price on the later of (i) the fundamental change repurchase date and (ii) the time of book-entry transfer or the delivery of the notes. If the paying agent holds money sufficient to pay the fundamental change repurchase price of the notes on the fundamental change repurchase date, then, with respect to the notes that have been properly surrendered for repurchase and have not been validly withdrawn:

- the notes will cease to be outstanding and interest will cease to accrue (whether or not book-entry transfer of the notes is made or whether or not the notes are delivered to the paying agent); and
- all other rights of the holder will terminate (other than the right to receive the fundamental change repurchase price).

In connection with any repurchase offer pursuant to a fundamental change repurchase notice, we will, if required:

- comply with the provisions of any tender offer rules under the Exchange Act that may then be applicable;
- file a Schedule TO or any other required schedule under the Exchange Act; and
- otherwise comply with all federal and state securities laws in connection with any offer by us to repurchase the notes,

in each case, so as to permit the rights and obligations under this Fundamental Change Permits Holders to Require Us to Repurchase Notes to be exercised in the time and in the manner specified in the indenture. To the extent that the provisions of any securities laws or regulations enacted after the date we initially issue the notes conflict with the provisions of the indenture relating to our obligations to purchase the notes upon a fundamental change, we will comply with the applicable securities laws and regulations and will not be deemed to have breached our obligations under such provisions of the indenture by virtue of such conflict.

No notes may be repurchased on any date at the option of holders upon a fundamental change if the principal amount of the notes has been accelerated, and such acceleration has not been rescinded, on or prior to such date (except in the case of an acceleration resulting from a default by us in the payment of the fundamental change repurchase price with respect to such notes).

The repurchase rights of the holders could discourage a potential acquirer of us. The fundamental change repurchase feature, however, is not the result of management s knowledge of any specific effort to obtain control of us by any means or part of a plan by management to adopt a series of anti-takeover provisions.

The term fundamental change is limited to specified transactions and may not include other events that might adversely affect our financial condition. In addition, the requirement that we offer to repurchase the notes upon a fundamental change may not protect holders in the event of a highly leveraged transaction, reorganization, merger or similar transaction involving us.

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Furthermore, holders may not be entitled to require us to repurchase their notes upon a fundamental change or entitled to an increase in the conversion rate upon conversion as described under Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change in circumstances involving a significant change in the composition of our board of directors unless such change is in connection with a fundamental change or make-whole fundamental change as described herein.

The definition of fundamental change includes a phrase relating to the sale, conveyance, lease or other transfer of all or substantially all of our consolidated assets. There is no precise, established definition of the phrase substantially all under applicable law. Accordingly, the ability of a holder of the notes to require us to repurchase its notes as a result of the sale, conveyance, lease or other transfer of less than all of our assets may be uncertain.

If a fundamental change were to occur, we may not have enough funds to pay the fundamental change repurchase price. Our ability to repurchase the notes for cash may be limited by restrictions on our ability to obtain funds for such repurchase through dividends from our subsidiaries, the terms of our then existing borrowing arrangements or otherwise. See Risk Factors Additional Risks Related to this Offering and the Notes We may not have the ability to raise the funds necessary to settle conversions of the notes or to repurchase the notes upon a fundamental change, and our future debt may contain limitations on our ability to repurchase the notes. If we fail to repurchase the notes when required following a fundamental change, we will be in default under the indenture. In addition, we may in the future incur other indebtedness with similar change in control provisions permitting our holders to accelerate or to require us to repurchase our indebtedness upon the occurrence of similar events or on some specific dates.

Consolidation, Merger or Sale of Assets

The indenture provides that we will not consolidate with or merge with or into, or sell, convey, transfer or lease all or substantially all of our properties and assets substantially as an entirety to, another person, if we are not the resulting, surviving or transferee person, unless (i) the resulting, surviving or transferee person is a corporation organized and existing under the laws of the United States of America, any State thereof or the District of Columbia, and such corporation expressly assumes by supplemental indenture all of our obligations under the notes and the indenture; and (ii) immediately after giving effect to such transaction, no default or event of default has occurred and is continuing under the indenture. Upon any such consolidation, merger or sale, conveyance, transfer or lease, the resulting, surviving or transferee person (if not us) shall succeed to, and may exercise every right and power of, ours under the indenture, and we will be discharged from our obligations under the notes and the indenture, except in the case of any such lease.

Although these types of transactions are permitted under the indenture, certain of the foregoing transactions could constitute a fundamental change permitting each holder to require us to repurchase the notes of such holder as described above.

Events of Default

Each of the following is an event of default with respect to the notes:

(1) default in any payment of interest on any note when due and payable and the default continues for a period of 30 days;

(2) default in the payment of principal of any note when due and payable at its stated maturity, upon redemption, upon any required repurchase, upon declaration of acceleration or otherwise;

(3) our failure to comply with our obligation to convert the notes in accordance with the indenture upon exercise of a holder s conversion right;

(4) our failure to give a fundamental change notice as described under Fundamental Change Permits Holders to Require Us to Repurchase Notes or notice of a specified corporate transaction as described

under Conversion upon Specified Corporate Events, in each case, such failure continues for three business days;

(5) our failure to comply with our obligations under Consolidation, Merger or Sale of Assets ;

(6) our failure for 60 days after written notice from the trustee or the holders of at least 25% in principal amount of the notes then outstanding has been received to comply with any of our other agreements contained in the notes or the indenture;

(7) default by us or any of our subsidiaries with respect to any mortgage, agreement or other instrument under which there may be outstanding, or by which there may be secured or evidenced, any indebtedness for money borrowed in excess of $30.0 million (or its foreign currency equivalent) in the aggregate of us and/or any such subsidiary, whether such indebtedness now exists or shall hereafter be created (i) resulting in such indebtedness becoming or being declared due and payable prior to its stated maturity or (ii) constituting a failure to pay the principal of any such indebtedness when due and payable at its stated maturity, upon required repurchase, upon declaration of acceleration or otherwise, and in the cases of clauses (i) and (ii) such acceleration shall not, after the expiration of any applicable grace period, have been rescinded or annulled or such failure to pay shall not have been cured or waived or such indebtedness shall not have been repaid, as the case may be, within 30 days; or

(8) a final judgment for the payment of $30.0 million or more (excluding any amounts covered by insurance) rendered against us or any of our significant subsidiaries (as defined below), which judgment is not discharged or stayed within 60 days after (i) the date on which the right to appeal thereof has expired if no such appeal has commenced, or (ii) the date on which all rights to appeal have been extinguished; or

(9) certain events of bankruptcy, insolvency, or reorganization of us or any of our significant subsidiaries.

A significant subsidiary is a subsidiary that is a significant subsidiary as defined in Article 1, Rule 1-02 of Regulation S-X promulgated by the SEC.

If an event of default occurs and is continuing, the trustee by notice to us, or the holders of at least 25% in principal amount of the outstanding notes by notice to us and the trustee, may declare 100% of the principal of and accrued and unpaid interest, if any, on all the notes to be due and payable. In case of certain events of bankruptcy, insolvency or reorganization involving us, 100% of the principal of and accrued and unpaid interest on the notes will automatically become due and payable. Upon such a declaration of acceleration, such principal and accrued and unpaid interest, if any, will be due and payable immediately.

Notwithstanding the foregoing, the indenture will provide that, to the extent we elect, the sole remedy for an event of default relating to (i) our failure to file with the trustee pursuant to Section 314(a)(1) of the Trust Indenture Act any documents or reports that we are required to file with the SEC pursuant to Section 13 or 15(d) of the Exchange Act or (ii) our failure to comply with our obligations as set forth under Reports below, will, for the first 360 days after the occurrence of such an event of default, consist exclusively of the right to receive additional interest on the notes at a rate equal to 0.25% per annum of the principal amount of the notes outstanding for each day during the first 90 days after the occurrence of such an event of default and 0.50% per annum of the principal amount of the notes outstanding

from the 91st day until the 360th day following the occurrence of such an event of default during which such event of default is continuing.

If we so elect, such additional interest will be payable in the same manner and on the same dates as the stated interest payable on the notes. On the 361st day after such event of default (if the event of default relating to the reporting obligations is not cured or waived prior to such 361st day), the notes will be subject to acceleration as provided above. The provisions of the indenture described in this paragraph will not affect the rights of holders of notes in the event of the occurrence of any other event of default. In the event we do not elect to pay the additional interest following an event of default in accordance with this paragraph or we elected to make such payment but do not pay the additional interest when due, the notes will be immediately subject to acceleration as provided above.

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In order to elect to pay the additional interest as the sole remedy during the first 360 days after the occurrence of an event of default relating to the failure to comply with the reporting obligations in accordance with the immediately preceding paragraph, we must notify all holders of the notes, the trustee and the paying agent of such election in writing prior to the beginning of such 360-day period. Upon our failure to timely give such notice, the notes will be immediately subject to acceleration as provided above.

In no event shall additional interest payable at our election for failure to comply with our reporting obligations pursuant to this Events of Default, accrue at a rate in excess of 0.50% per annum pursuant to the indenture, regardless of the number of events or circumstances giving rise to the requirement to pay such additional interest.

If any portion of the amount payable on the notes upon acceleration is considered by a court to be unearned interest (through the allocation of the value of the instrument to the embedded warrant or otherwise), the court could disallow recovery of any such portion.

The holders of a majority in principal amount of the outstanding notes may waive all past defaults (except with respect to any continuing defaults relating to nonpayment of principal or interest or with respect to the failure to deliver the consideration due upon conversion) and rescind any such acceleration with respect to the notes and its consequences if (i) rescission would not conflict with any judgment or decree of a court of competent jurisdiction and (ii) all existing events of default, other than the nonpayment of the principal of and interest on the notes or failure to deliver amounts due upon conversion, have been cured or waived.

Each holder shall have the right to receive payment or delivery, as the case may be, of:

the principal (including the redemption price and fundamental change repurchase price, if applicable) of;

accrued and unpaid interest, if any, on; and

the consideration due upon conversion of,

its notes, on or after the respective due dates expressed or provided for in the indenture, or to institute suit for the enforcement of any such payment or delivery, as the case may be, and such right to receive such payment or delivery, as the case may be, on or after such respective dates shall not be impaired or affected without the consent of such holder.

If an event of default occurs and is continuing, the trustee will be under no obligation to exercise any of the rights or powers under the indenture at the request or direction of any of the holders unless such holders have offered to the trustee indemnity or security satisfactory to it against any loss, liability or expense. Except to enforce the right to receive payment of principal or interest when due, or the right to receive payment or delivery of the consideration due upon conversion, no holder may pursue any remedy with respect to the indenture or the notes unless:

(1) such holder has previously given the trustee written notice that an event of default is continuing;

(2) holders of at least 25% in principal amount of the outstanding notes have requested the trustee to pursue the remedy;

(3) such holders have offered the trustee security or indemnity satisfactory to it against any loss, liability or expense;

(4) the trustee has not complied with such request within 60 days after the receipt of the request and the offer of security or indemnity; and

(5) the holders of a majority in principal amount of the outstanding notes have not given the trustee a direction that, in the opinion of the trustee, is inconsistent with such request within such 60-day period.

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Subject to certain restrictions, the holders of a majority in principal amount of the outstanding notes are given the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or of exercising any trust or power conferred on the trustee.

The indenture provides that in the event an event of default has occurred and is continuing, the trustee will be required in the exercise of its powers to use the degree of care that a prudent person would use in the conduct of its own affairs. The trustee, however, may refuse to follow any direction that conflicts with law or the indenture or that the trustee determines is unduly prejudicial to the rights of any other holder or that would involve the trustee in personal liability. Prior to taking any action under the indenture, the trustee will be entitled to indemnification or security satisfactory to it against any loss, liability or expense caused by taking or not taking such action.

The indenture provides that if a default occurs with respect to the notes and is continuing and is actually known to the trustee, the trustee must send to each holder notice of the default within 90 days after it receives notice thereof. Except in the case of a default in the payment of principal of or interest on any note or a default in the payment or delivery of the consideration due upon conversion, the trustee may withhold notice if and so long as it in good faith determines that withholding notice is in the interests of the holders. In addition, we are required to deliver to the trustee, within 120 days after the end of each fiscal year, a certificate indicating whether the signers thereof know of any default that occurred during the previous year. We are also required to deliver to the trustee, within 30 days after the occurrence thereof, written notice of any events which would constitute certain defaults, their status and what action we are taking or proposing to take in respect thereof.

Payments of the redemption price, fundamental change repurchase price, principal and interest that are not made when due will accrue interest per annum at the then-applicable, interest rate from the required payment date.

Modification and Amendment

Subject to certain exceptions, the indenture or the notes may be amended with the consent of the holders of at least a majority in principal amount of the notes then outstanding (including without limitation, consents obtained in connection with a repurchase of, or tender or exchange offer for, notes) and, subject to certain exceptions, any past default or compliance with any provisions may be waived with the consent of the holders of a majority in principal amount of such notes then outstanding (including, connection with a repurchase of, or tender or exchange offer for, notes). However, without the consent of each holder of an outstanding note affected, no amendment may, among other things:

(1) reduce the amount of notes whose holders must consent to an amendment;

(2) reduce the rate of or extend the stated time for payment of interest on any note;

(3) reduce the principal of or extend the stated maturity of any note;

(4) except as required under the indenture, make any change that adversely affects the conversion rights of any notes;

(5) reduce the redemption price, the fundamental change repurchase price of any note or amend or modify in any manner adverse to the holders of notes our obligation to make such payments, whether through an amendment or waiver of provisions in the covenants, definitions or otherwise;

(6) make any note payable in money other than that stated in such note;

(7) change the ranking of the notes;

(8) impair the right of any holder to receive payment of principal and interest on such holder s notes on or after the due dates therefor or to institute suit for the enforcement of any payment on or with respect to such holder s notes; or

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(9) make any change in the amendment provisions that require each holder s consent or in the waiver provisions.

Without the consent of any holder, we and the trustee may amend the indenture to:

(1) cure any ambiguity, omission, defect or inconsistency;

(2) provide for the assumption by a successor corporation of our obligations under the indenture;

(3) add guarantees with respect to the notes;

(4) secure the notes;

(5) add to our covenants or events of default for the benefit of the holders or surrender any right or power conferred upon us;

(6) make any change that does not adversely affect the rights of any holder;

(7) increase the conversion rate as provided in the indenture;

(8) provide for the acceptance of appointment by a successor trustee or facilitate the administration of the trusts under the indenture by more than one trustee;

(9) in connection with any merger event described under Conversion Rights Recapitalizations, Reclassifications and Changes of Our Common Stock above, provide that the notes are convertible into reference property, subject to the provisions described under Conversion Rights Settlement upon Conversion above, and make certain related changes to the terms of the notes to the extent expressly required by the indenture;

(10) comply with the rules of any applicable securities depositary in a manner that does not adversely affect the rights of any holder;

(11) to make provisions with respect to conversion rights of the holders of the notes as required under the indenture;

(12) conform the provisions of the indenture to any provision of the Description of Notes in the preliminary prospectus supplement, as supplemented by the related pricing term sheet; or

(13) comply with any requirement of the SEC in connection with the qualification of the indenture under the Trust Indenture Act.

Holders do not need to approve the particular form of any proposed amendment. It will be sufficient if such holders approve the substance of the proposed amendment. After an amendment under the indenture becomes effective, we are required to deliver to the holders (with a copy to the trustee) a notice briefly describing such amendment. However, the failure to give such notice to all the holders (with a copy to the trustee), or any defect in the notice, will not impair or affect the validity of the amendment.

Discharge

We may satisfy and discharge our obligations under the indenture and the notes by delivering to the securities registrar for cancellation all outstanding notes or by depositing with the trustee or delivering to the holders, as applicable, after the notes have become due and payable, whether at maturity, any redemption date, any fundamental change repurchase date, upon conversion or otherwise, cash or cash and/or shares of common stock (solely to satisfy outstanding conversions, as applicable) sufficient to pay all of the outstanding notes and paying all other sums payable under the indenture by us. Such discharge is subject to terms contained in the indenture.

Calculations in Respect of the Notes

Except as otherwise provided above, we will be responsible for making all calculations called for under the notes. These calculations include, but are not limited to, determinations of the stock price, the last reported sale

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prices of our common stock, the trading price of the notes (for purposes of determining whether the notes are convertible as described herein) the daily VWAPs, the daily conversion values, the daily settlement amounts, redemption conversion values, redemption prices, accrued interest payable on the notes and the conversion rate of the notes. We will make all these calculations in good faith and, absent manifest error, our calculations will be final and binding on holders of notes. We will provide a schedule of our calculations to each of the trustee and the conversion agent, and each of the trustee and the conversion agent is entitled to rely conclusively upon the accuracy of our calculations without independent verification. We will forward our calculations to any holder of notes upon the written request of that holder. Neither the trustee nor the conversion agent shall be responsible and assume any liability for any calculations under the notes.

Reports

The indenture provides that any documents or reports that we are required to file with the SEC pursuant to Section 13 or 15(d) of the Exchange Act (excluding any such information, documents or reports, or portions thereof, subject to confidential treatment and any correspondence with the SEC) must be filed by us with the trustee within 15 days after the same are required to be filed with the SEC (giving effect to any grace period provided by Rule 12b-25 or any successor rule under the Exchange Act). Documents filed by us with the SEC via the EDGAR (or any successor thereto) system will be deemed to be filed with the trustee as of the time such documents are filed via EDGAR (or any successor thereto), it being understood that the trustee shall not be responsible for determining whether such filings have been made. Delivery of reports, information and documents to the trustee under the indenture is for informational purposes only and the information and the trustee s receipt of the foregoing shall not constitute constructive notice of any information contained therein, or determinable from information contained therein including our compliance with any of its covenants thereunder (as to which the trustee is entitled to rely exclusively on an officer s certificate).

Trustee

U.S. Bank, National Association is the initial trustee, security registrar, paying agent and conversion agent for the notes.

U.S. Bank, National Association in each of its capacities, including without limitation as trustee, security registrar, paying agent and conversion agent, assumes no responsibility for the accuracy or completeness of the information concerning us or our affiliates or any other party contained in this document or the related documents or for any failure by us or any other party to disclose events that may have occurred and may affect the significance or accuracy of such information. The trustee shall not be responsible for and makes no representations as to the validity or adequacy of the indenture or the notes and it shall not be accountable for our use of the proceeds from the notes, and it shall not be responsible for any statement in any offering memorandum, prospectus or other disclosure materials distributed with respect to the notes (other than information provided by the trustee concerning the trustee).

Governing Law

The indenture provides that it and the notes, and any claim, controversy or dispute arising under or related to the indenture or the notes, will be governed by and construed in accordance with the laws of the State of New York (without regard to the conflicts of laws provisions thereof).

Book-Entry, Settlement and Clearance

The Global Notes

The notes will be initially issued in the form of one or more registered notes in global form, without interest coupons (the global notes). Upon issuance, each of the global notes will be deposited with the trustee as custodian for DTC and registered in the name of Cede & Co., as nominee of DTC.

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Ownership of beneficial interests in a global note will be limited to persons who have accounts with DTC (DTC participants) or persons who hold interests through DTC participants. We expect that under procedures established by DTC:

- upon deposit of a global note with DTC s custodian, DTC will credit portions of the principal amount of the global note to the accounts of the DTC participants designated by the underwriter; and
- ownership of beneficial interests in a global note will be shown on, and transfer of ownership of those interests will be effected only through, records maintained by DTC (with respect to interests of DTC participants) and the records of DTC participants (with respect to other owners of beneficial interests in the global note).

Beneficial interests in global notes may not be exchanged for notes in physical, certificated form except in the limited circumstances described below.

Book-Entry Procedures for the Global Notes

All interests in the global notes will be subject to the operations and procedures of DTC. We provide the following summary of those operations and procedures solely for the convenience of investors. The operations and procedures of DTC are controlled by that settlement system and may be changed at any time. Neither we nor the underwriter are responsible for those operations or procedures.

DTC has advised us that it is:

- a limited purpose trust company organized under the laws of the State of New York;
- a banking organization within the meaning of the New York State Banking Law;
- a member of the Federal Reserve System;
- a clearing corporation within the meaning of the Uniform Commercial Code; and
- a clearing agency registered under Section 17A of the Exchange Act.

DTC was created to hold securities for its participants and to facilitate the clearance and settlement of securities transactions between its participants through electronic book-entry changes to the accounts of its participants. DTC s participants include securities brokers and dealers, including the underwriter; banks and trust companies; clearing corporations and other organizations. Indirect access to DTC s system is also available to others such as banks, brokers, dealers and trust companies; these indirect participants clear through or maintain a custodial relationship with a DTC participant, either directly or indirectly. Investors who are not DTC participants may beneficially own securities held by or on behalf of DTC only through DTC participants or indirect participants in DTC.

So long as DTC s nominee is the registered owner of a global note, that nominee will be considered the sole owner or holder of the notes represented by that global note for all purposes under the indenture. Except as provided below, owners of beneficial interests in a global note:

- will not be entitled to have notes represented by the global note registered in their names;
- will not receive or be entitled to receive physical, certificated notes; and
- will not be considered the owners or holders of the notes under the indenture for any purpose, including with respect to the giving of any direction, instruction or approval to the trustee under the indenture.

As a result, each investor who owns a beneficial interest in a global note must rely on the procedures of DTC to exercise any rights of a holder of notes under the indenture (and, if the investor is not a participant or an indirect participant in DTC, on the procedures of the DTC participant through which the investor owns its interest). Neither we nor the trustee, paying agent or conversion agent has any responsibility or liability for any act or omission of DTC.

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Payments of principal and interest with respect to the notes represented by a global note will be made by the trustee to DTC s nominee as the registered holder of the global note. Neither we nor the trustee or the paying agent will have any responsibility or liability for the payment of amounts to owners of beneficial interests in a global note, for any aspect of the records relating to or payments made on account of those interests by DTC, or for maintaining, supervising or reviewing any records of DTC relating to those interests.

Payments by participants and indirect participants in DTC to the owners of beneficial interests in a global note will be governed by standing instructions and customary industry practice and will be the responsibility of those participants or indirect participants and DTC.

Transfers between participants in DTC will be effected under DTC s procedures and will be settled in same-day funds.

Certificated Notes

Notes in physical, certificated form will be issued and delivered to each person that DTC identifies as a beneficial owner of the related notes only if:

DTC notifies us at any time that it is unwilling or unable to continue as depositary for the global notes and a successor depositary is not appointed within 90 days;

DTC ceases to be registered as a clearing agency under the Exchange Act and a successor depositary is not appointed within 90 days; or

an event of default with respect to the notes has occurred and is continuing and such beneficial owner requests that its notes be issued in physical, certificated form.

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DESCRIPTION OF SHARE LENDING AGREEMENT

Concurrently with this offering, up to 30,000,000 of shares of our common stock will be offered, by means of a separate prospectus supplement and accompanying prospectus, by the selling stockholders named therein (which may include the underwriter or its affiliates), who will borrow such shares through lending arrangements from an affiliate of the underwriter, which is borrowing the shares, as Share Borrower, from us. The borrowed shares were issued by us to facilitate this lending arrangement. The borrowed shares are newly-issued shares issued in connection with this transaction and will be cancelled or held as treasury shares by us upon the expiration or the early termination of the share lending arrangements. As of the date of this prospectus supplement, taking into account the maximum number of shares that may be issued in connection with this share lending arrangement, we would have 616,331,543 shares issued and outstanding. None of the Share Borrower, its affiliates or us will receive any proceeds of the offering or sale of the borrowed shares, except to the extent the underwriter or any of its affiliates is named as a selling stockholder or as otherwise described below.

To make the purchase of the notes offered pursuant to this prospectus supplement more attractive to prospective investors, we have agreed to make the borrowed shares available to the Share Borrower which will, in turn, make the borrowed shares available to the selling stockholders as described above. With respect to borrowed shares sold by selling stockholders concurrently with, or shortly following, the offering of the notes, the share lending arrangements with the Share Borrower will be available during a period beginning on the date of the closing of this offering and ending on or about the maturity date of the notes, or, if earlier, on or about the date as of which all of the notes cease to be outstanding as a result of redemption, repurchase, conversion or other acquisition for value (or earlier in certain circumstances) (the loan availability period).

Share loans under the share lending agreement with the Share Borrower will terminate, and the borrowed shares thereunder must be returned to us if the concurrent offering of the notes is not consummated or upon the termination of the loan availability period with respect to such share lending agreement, as well as under the following circumstances:

- the Share Borrower may terminate all or any portion of a loan under the share lending agreement at any time;
- after the date on which all of the notes are repurchased, converted or otherwise acquired for value; and
- the Share Borrower or we may terminate any or all of the applicable outstanding loans upon certain defaults by the other party under the share lending agreement, including certain breaches of representations, warranties, covenants or agreements under the share lending agreement, or the bankruptcy of the Share Borrower or us.

The holders of the borrowed shares will have the right to vote the shares on all matters submitted to a vote of our stockholders and the right to receive any dividends or other distributions that we may pay or make on outstanding shares of our common stock. However, under the share lending agreement, the Share Borrower has agreed:

- to pay to us an amount equal to cash dividends, if any, that we pay on the borrowed shares;

to pay or deliver, as the case may be, to us any other distribution, other than in a liquidation or a reorganization in bankruptcy, that we make on the borrowed shares; and

not to vote on the borrowed shares on any matter submitted to a vote of our stockholders, except in certain circumstances where such vote is required for quorum purposes.

We expect that the selling stockholders will sell the borrowed shares and use the resulting short position to establish their initial hedge with respect to their respective investments in the notes. The selling stockholders may short sell up to the number of borrowed shares concurrently with, or shortly following, the offering of the notes. The total number of shares that the selling stockholders can borrow under the share lending agreement is limited to a maximum of 30,000,000 shares. The selling stockholders may effect such transactions by selling the borrowed

shares at various prices from time to time through the underwriter or its affiliates, which may receive compensation in the form of discounts, concessions or commissions from the selling stockholders and/or from purchasers of borrowed shares for whom the underwriter may act as agent or to whom it may sell as principal. In addition, the Share Borrower has agreed to pay a nominal fee to us in connection with the issuances of the borrowed shares. The existence of the share lending agreement and the short sales of our common stock effected in connection with the sale of the notes being offered concurrently herewith could cause the market price of our common stock to be lower over the term of the share lending agreement than it would have been if there was no such agreement. See Risk Factors Additional Risks Related to the Offering and the Notes Future sales of our common stock, as well as sales of the borrowed shares in the concurrent offering, or the issuance of other equity-related securities could lower the market price for our common stock and adversely impact the trading price of the notes. However, we have determined that our entry into the share lending agreement is in our best interests as a means to facilitate the offer and sale of the notes pursuant to the related prospectus supplement and accompanying prospectus on terms more favorable to us than we could have otherwise obtained. The concurrent offering of the borrowed shares is conditioned upon the closing of this offering.

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DESCRIPTION OF OTHER INDEBTEDNESS

BioReference Credit Agreement and Lines of Credit

On November 5, 2015, BioReference and certain of its subsidiaries entered into a credit agreement with JPMorgan Chase Bank, N.A. (CB) as lender and administrative agent, as amended (the Credit Agreement). The Credit Agreement provides for a $175.0 million secured revolving credit facility and includes a $20.0 million sub-facility for swingline loans and a $20.0 million sub-facility for the issuance of letters of credit. BioReference may increase the credit facility to up to $275.0 million on a secured basis, subject to the satisfaction of specified conditions. The Credit Agreement matures on November 5, 2020 and is guaranteed by all of BioReference s domestic subsidiaries. The Credit Agreement is also secured by substantially all assets of BioReference and its domestic subsidiaries, as well as a non-recourse pledge by us of our equity interest in BioReference. Availability under the Credit Agreement is based on a borrowing base comprised of eligible accounts receivables of BioReference and certain of its subsidiaries, as specified therein.

On March 17, 2017, BioReference and certain of its subsidiaries entered into Amendment No. 3 to the Credit Agreement, which amended the Credit Agreement to permit BioReference and its subsidiaries to dividend cash to us in the form of an intercompany loan, in an aggregate amount not to exceed $55.0 million. On August 7, 2017, BioReference and certain of its subsidiaries entered into Amendment No. 4 to the Credit Agreement, which amended the Credit Agreement to permit BioReference and its subsidiaries to dividend cash to us in the form of an additional intercompany loan, in an aggregate amount not to exceed $35.0 million. On November 8, 2017, BioReference and certain of its subsidiaries entered into Amendment No. 5 to the Credit Agreement, which amended the Credit Agreement to, among other things, ease certain thresholds that require increased reporting by BioReference and reduce the pro forma availability condition for BioReference to make certain cash dividends to us. On December 22, 2017, BioReference and certain of its subsidiaries entered into Amendment No. 6 to the Credit Agreement, which amended the Credit Agreement to, among other things, permit BioReference and its subsidiaries to dividend cash to us in the form of intercompany loans, in an aggregate amount not to exceed $45.0 million. The other terms of the Credit Agreement remain unchanged.

On February 28, 2018, BioReference and certain of its subsidiaries entered into Amendment No. 7 to the Credit Agreement, which amended the Credit Agreement to permit BioReference and its subsidiaries to use cash on hand, up to a maximum amount set forth in the amendment, to meet the availability requirements that otherwise would trigger (i) covenants that would require BioReference to maintain a minimum fixed charge coverage ratio and provide certain increased reporting under the Credit Agreement and (ii) CB s right, as agent for the lenders under the Credit Agreement, to exercise sole dominion over funds held in certain accounts of BioReference. The other terms of the Credit Agreement remain unchanged.

The Credit Agreement contains customary covenants and restrictions, including, without limitation, covenants that require BioReference and its subsidiaries to maintain a minimum fixed charge coverage ratio if availability under the Credit Agreement falls below a specified amount and to comply with laws and restrictions on the ability of BioReference and its subsidiaries to incur additional indebtedness or to pay dividends and make certain other distributions to us, subject to certain exceptions as specified therein. Failure to comply with these covenants would constitute an event of default under the Credit Agreement, notwithstanding the ability of BioReference to meet its debt service obligations. The Credit Agreement also includes various customary remedies for the lenders following an event of default, including the acceleration of repayment of outstanding amounts under the Credit Agreement and execution upon the collateral securing obligations under the Credit Agreement. Substantially all the assets of BioReference and its subsidiaries are restricted from sale, transfer, lease, disposal or distributions to us, subject to certain exceptions. BioReference and its subsidiaries net assets as of September 30, 2018 were approximately

$0.9 billion, which includes goodwill of $401.8 million and intangible assets of $415.2 million.

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In addition to the Credit Agreement with CB, we have line of credit agreements with twelve other financial institutions as of September 30, 2018 in the U.S., Chile and Spain. These lines of credit are used primarily as a source of working capital for inventory purchases.

As of September 30, 2018, the total availability under the Credit Agreement and our lines of credit with financial institutions in Chile and Spain was $138.0 million, of which $109.7 million was used and outstanding as of September 30, 2018. The weighted average interest rate on these lines of credit is approximately 4.7%. These lines of credit are short-term and are used primarily as a source of working capital. We intend to continue to enter into these lines of credit as needed. There is no assurance that these lines of credit or other funding sources will be available to us on acceptable terms, or at all, in the future.

5% Convertible Promissory Notes

In February 2018, we issued a series of 5% Convertible Promissory Notes (the 2023 Convertible Notes) in the aggregate principal amount of $55.0 million. The 2023 Convertible Notes mature five years from the date of issuance. Each holder of a 2023 Convertible Note has the option, from time to time, to convert all or any portion of the outstanding principal balance of such 2023 Convertible Note, together with accrued and unpaid interest thereon, into shares of our common stock at a conversion price of $5.00 per share of common stock. We may redeem all or any part of the then issued and outstanding 2023 Convertible Notes, together with accrued and unpaid interest thereon, pro ratably among the holders, upon no fewer than 30 days, and no more than 60 days, notice to the holders. The 2023 Convertible Notes contain customary events of default and representations and warranties of OPKO. As of September 30, 2018, $55.0 million principal was outstanding under the 2023 Convertible Notes.

2033 Senior Notes

On January 30, 2013, we issued $175.0 million in original principal amount of 3.00% Senior Convertible Notes (the 2033 Senior Notes) to qualified institutional buyers and accredited investors in a private placement in reliance on exemptions from registration under the Securities Act. The 2033 Senior Notes bear interest at the rate of 3.00% per year, payable semiannually on February 1 and August 1 of each year. The 2033 Senior Notes will mature on February 1, 2033, unless earlier repurchased, redeemed or converted. Upon a fundamental change as defined in the Indenture, dated as of January 30, 2013, by and between us and Wells Fargo Bank N.A., as trustee, governing the 2033 Senior Notes (the 2033 Indenture), subject to certain exceptions, the holders may require us to repurchase all or any portion of their 2033 Senior Notes for cash at a repurchase price equal to 100% of the principal amount of the 2033 Senior Notes being repurchased, plus any accrued and unpaid interest to but not including the related fundamental change repurchase date. As of September 30, 2018, $31.8 million principal was outstanding under the 2033 Convertible Notes.

The 2033 Senior Notes will be convertible at any time on or after November 1, 2032, through the second scheduled trading day immediately preceding the maturity date, at the option of the holders. Additionally, holders may convert their 2033 Senior Notes prior to the close of business on the scheduled trading day immediately preceding November 1, 2032, under the following circumstances: (1) conversion based upon satisfaction of the trading price condition relating to the 2033 Senior Notes; (2) conversion based on the common stock price; (3) conversion based upon the occurrence of specified corporate events; or (4) if we call the 2033 Senior Notes for redemption. The 2033 Senior Notes will be convertible into cash, shares of our common stock, or a combination of cash and shares of common stock, at our election unless we have made an irrevocable election of net share settlement. The initial conversion rate for the 2033 Senior Notes will be 141.48 shares of common stock per $1,000 principal amount of 2033 Senior Notes (equivalent to an initial conversion price of approximately $7.07 per share of common stock), and will be subject to adjustment upon the occurrence of certain events. In addition, we will, in certain circumstances,

increase the conversion rate for holders who convert their 2033 Senior Notes in connection with a make-whole fundamental change (as defined in the 2033 Indenture). Holders of the 2033 Senior Notes may require us to repurchase the 2033 Senior Notes for 100% of their principal amount,

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plus accrued and unpaid interest, on February 1, 2019, February 1, 2023 and February 1, 2028, or following the occurrence of a fundamental change (as defined in the 2033 Indenture). As of September 30, 2018, $31.8 million aggregate principal amount was outstanding under the 2033 Senior Notes. On February 1, 2019, approximately $28.8 million aggregate principal amount of 2033 Senior Notes were tendered by holders thereof pursuant to such holders option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes. The aggregate repurchase price for such 2033 Senior Notes is the aggregate principal amount of such 2033 Senior Notes, plus accrued and unpaid interest thereon to, but not including, the date of repurchase. Following the repurchase, approximately $3.1 million aggregate principal amount of the 2033 Senior Notes will remain outstanding.

On or after February 1, 2019, we may redeem for cash any or all of the 2033 Senior Notes at a redemption price of 100% of the principal amount of the 2033 Senior Notes to be redeemed, plus any accrued and unpaid interest up to but not including the redemption date.

The terms of the 2033 Senior Notes, include, among others: (i) rights to convert into shares of our common stock, including upon a fundamental change; and (ii) a coupon make-whole payment in the event of a conversion by the holders of the 2033 Senior Notes on or after February 1, 2017 but prior to February 1, 2019.

Line of Credit with Dr. Frost

On November 8, 2018, we entered into a credit agreement with an affiliate of Dr. Frost, pursuant to which the lender committed to provide us with an unsecured line of credit in the amount of $60 million. Borrowings under the line of credit will bear interest at a rate of 10% per annum and may be repaid and reborrowed at any time. The credit agreement includes various customary remedies for the lender following an event of default, including the acceleration of repayment of outstanding amounts under line of credit. The line of credit matures on November 8, 2023.

On February 1, 2019, we borrowed $28.8 million under the line of credit; no amounts were previously outstanding under the line of credit. We intend to use the proceeds of the $28.8 million borrowing to repurchase the 2033 Senior Notes tendered by holders thereof pursuant to such holders option to require us to repurchase such 2033 Senior Notes pursuant to the terms of the indenture governing the 2033 Senior Notes. The aggregate repurchase price for such 2033 Senior Notes is the aggregate principal amount of such 2033 Senior Notes, plus accrued and unpaid interest thereon to, but not including, the date of repurchase. We intend to use a portion of the proceeds of this offering to repay the $28.8 million principal amount and accrued but unpaid interest currently outstanding under the line of credit and to terminate the line of credit thereafter.

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U.S. FEDERAL INCOME TAX CONSIDERATIONS

This section is a discussion of certain material U.S. federal income tax considerations relating to the ownership, disposition and conversion of the notes and the ownership and disposition of the common stock into which the notes may be converted. This summary does not provide a complete analysis of all potential tax considerations. The information provided below is based on existing U.S. federal income tax authorities, all of which are subject to change or differing interpretations, possibly with retroactive effect. There can be no assurances that the Internal Revenue Service (the IRS) will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, a ruling from the IRS with respect to the U.S. federal income tax consequences of owning, disposing of or converting the notes or of owning or disposing of the common stock into which the notes may be converted. The summary generally applies only to beneficial owners of the notes that purchase their notes in this offering for an amount equal to the issue price of the notes (generally, the first price at which a substantial amount of the notes is sold for money to investors (not including sales to bond houses, brokers or similar persons or organizations acting in the capacity of underwriters, placement agents or wholesalers)) and that hold the notes and common stock as capital assets within the meaning of Section 1221 of the Internal Revenue Code of 1986, as amended (the Code) (generally, property held for investment).

This discussion does not purport to deal with all aspects of U.S. federal income taxation that may be relevant to a particular beneficial owner in light of the beneficial owner s circumstances or status. Also, it is not intended to apply to beneficial owners which may be subject to special rules (including, without limitation, partnerships and pass-through entities and investors in such entities, dealers in securities, traders in securities that elect to use a mark-to-market method of tax accounting, banks, thrifts, regulated investment companies, real estate investment trusts, insurance companies, tax-exempt entities, tax-deferred or other retirement accounts, persons subject to the alternative minimum tax provisions of the Code, U.S. Holders (as defined below) whose functional currency is not the U.S. dollar, U.S. Holders who hold notes through a non-U.S. broker or other non-U.S. intermediary, controlled foreign corporations, passive foreign investment companies, certain former citizens or long-term residents of the United States, expatriated entities subject to Section 7874 of the Code, non-U.S. Holders (as defined below) that are estates or trusts and that have one or more U.S. beneficiaries, persons holding notes or common stock as part of a hedging, conversion or integrated transaction or a straddle, corporations that accumulate earnings to avoid U.S. federal income tax, persons deemed to sell notes or common stock under the constructive sale provisions of the Code, or persons subject to special tax rules under Section 451(b) of the Code). This summary does not address the potential application of the Medicare contribution tax on net investment income imposed by Section 1411 of the Code, the rules applicable to qualified small business stock under Section 1202 of the Code, the effects of the U.S. federal estate and gift tax laws or any applicable non-U.S., state or local laws.

THE FOLLOWING DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT A SUBSTITUTE FOR CAREFUL TAX PLANNING AND ADVICE. INVESTORS CONSIDERING THE PURCHASE OF NOTES SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AND THE CONSEQUENCES OF U.S. FEDERAL ESTATE OR GIFT TAX LAWS, NON-U.S., STATE AND LOCAL LAWS AND TAX TREATIES.

As used herein, the term U.S. Holder means a beneficial owner of a note or the common stock into which the notes may be converted that, for U.S. federal income tax purposes, is (1) an individual who is a citizen or resident of the United States, (2) a corporation, or an entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state of the United States, or the District of Columbia, (3) an estate the income of which is subject to U.S. federal income taxation regardless of its source, or (4) a trust if it (x) is subject to the primary supervision of a U.S. court and the control of one of more U.S. persons or (y) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

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A non-U.S. Holder is a beneficial owner of a note or the common stock into which the notes may be converted (other than an entity or arrangement treated as a partnership for U.S. federal income tax purposes) that is not a U.S. Holder.

If an entity or arrangement, domestic or foreign, treated as a partnership for U.S. federal income tax purposes is a beneficial owner of a note or common stock acquired upon conversion of a note, the tax treatment of a partner in the partnership will depend upon the status of the partner and the activities of the partner and the partnership. A beneficial owner of a note or common stock acquired upon conversion of a note that is treated as a partnership for U.S. federal income tax purposes, and partners in such an entity, should consult their own tax advisors about the U.S. federal income tax consequences of purchasing, owning and disposing of such note or common stock.

Additional Amounts

We may be required to make payments of additional amounts on a note in certain circumstances, such as those described under Description of Notes Events of Default . We intend to take the position that this possible payment of such additional amounts will not subject the notes to the special rules governing certain contingent payment debt instruments under the applicable Treasury Regulations (which, if applicable, could materially and adversely affect the timing, amount and character of income with respect to the notes), based on our determination that there is only a remote possibility that we would be required to make any additional payments, that if such additional payments were required to be paid, they would be an incidental amount, or that such additional payments are otherwise disregarded for purposes of these rules. Our determination that the notes are not contingent payment debt instruments is binding on U.S. Holders unless they disclose their contrary position in the manner required by applicable Treasury Regulations. However, our determination is not binding on the IRS, which may take a position contrary to our position, in which case the timing, amount and character of income recognized may differ adversely from the consequences discussed herein, including accrual of interest income at a rate higher than the stated interest rate and treatment of gain on disposition (including all gain realized upon conversion) as interest income rather than capital gain. The remainder of this discussion assumes that the notes are not treated as contingent payment debt instruments subject to such rules. U.S. Holders and non-U.S. Holders are urged to consult their own tax advisers regarding the potential application to the notes of the contingent payment debt regulations and the consequences thereof.

U.S. Holders

Taxation of Interest

U.S. Holders will be required to recognize as ordinary income any stated interest that is paid or accrued on the notes, in accordance with their regular method of tax accounting for U.S. federal income tax purposes.

In general, if the terms of a debt instrument entitle a holder to receive payments (other than certain fixed periodic interest payments) that exceed the issue price of the instrument by at least a statutorily defined de minimis amount, the U.S. Holder will be required to include such excess in income as original issue discount over the term of the instrument on a constant yield to maturity basis, irrespective of the U.S. Holder s regular method of tax accounting. We expect, and the discussion below assumes, that the notes will not be issued with original issue discount for U.S. federal income tax purposes.

Sale, Exchange, Redemption or Other Taxable Disposition of Notes

A U.S. Holder generally will recognize capital gain or loss if the U.S. Holder disposes of a note in a sale, exchange, redemption or other taxable disposition (other than conversion of a note into either shares of our common stock or a combination of cash and shares of our common stock, the U.S. federal income tax consequences of which are

described under Conversion of Notes below). The U.S. Holder s gain or loss will

equal the difference between the amount realized by the U.S. Holder (other than amounts attributable to accrued but unpaid interest which would be subject to tax as described above under Taxation of Interest) and its adjusted tax basis in the note. The amount realized by the U.S. Holder will include the amount of any cash and the fair market value of any other property received for the note. The U.S. Holder s adjusted tax basis in the note generally will equal the amount it paid for the note, reduced by the amount of any payments received by the U.S. Holder on the note other than stated interest. The portion of any amount realized that is attributable to accrued and unpaid interest will not be taken into account in computing the U.S. Holder s capital gain or loss. Instead, that portion will be recognized as ordinary interest income to the extent that the U.S. Holder has not previously included the accrued interest in income. The gain or loss recognized by the U.S. Holder on the disposition of the note generally will be long-term capital gain or loss if it held the note for more than one year, or short-term capital gain or loss if it held the note for one year or less, at the time of the transaction. Long-term capital gains of non-corporate taxpayers generally are taxed at reduced rates. Short-term capital gains are taxed at ordinary income rates. The deductibility of capital losses is subject to limitations.

Conversion of Notes

Upon conversion of a note solely into cash, a U.S. Holder generally will be subject to the rules described under Sale, Exchange, Redemption or Other Taxable Disposition of Notes above, subject to the discussion under Constructive Distributions below regarding the possibility that certain adjustments to the conversion rate of a note may be treated as a taxable dividend.

A U.S. Holder generally will not recognize any income, gain or loss on the conversion of a note solely into shares of our common stock, except with respect to cash received in lieu of a fractional share of common stock and the fair market value of any common stock attributable to accrued and unpaid interest, subject to the discussion below under Constructive Distributions regarding the possibility that certain adjustments to the conversion rate of a note may be treated as a taxable dividend. The U.S. Holder s tax basis in the common stock received upon conversion of a note (including any fractional share for which cash is paid, but excluding shares attributable to accrued and unpaid interest) will equal the U.S. Holder s adjusted tax basis in the note that was converted. The U.S. Holder s holding period in the common stock received (other than shares attributable to accrued and unpaid interest which will commence on the day after receipt) will include the holding period in the converted note.

The tax consequences of the conversion of a note into a combination of cash and shares of our common stock are not entirely clear. If the note constitutes a security for U.S. federal income tax purposes, a U.S. Holder may be treated as exchanging the note for our common stock and cash in a recapitalization for U.S. federal income tax purposes. The term security is not defined in the Code or in the Treasury Regulations, and has not been clearly defined by judicial decisions. An instrument is a security for these purposes if, based on all the facts and circumstances, the instrument constitutes a meaningful investment in the issuer of the instrument. Although there are a number of factors that may affect the determination of whether a debt instrument is a security, one of the most important factors is the original term of the instrument, or the length of time between the issuance of the instrument and its maturity. In general, instruments with an original term of more than ten years are likely to be treated as securities, and instruments with an original term of less than five years may not be treated as securities. In addition, the convertibility of a debt instrument into stock of the issuer may argue in favor of security treatment because of the possible equity participation in the issuer. We intend to take the position that the notes are securities and that the conversion of a note into a combination of cash and shares of our common stock is treated as a recapitalization, in each case, for U.S. federal income tax purposes, although there can be no assurance in this regard.

If the note is a security and the conversion of a note into a combination of cash and shares of our common stock is treated as a recapitalization for U.S. federal income tax purposes, the U.S. Holder would not be permitted to recognize loss, but would be required to recognize gain, if any. The amount of gain recognized by a U.S. Holder generally would

equal the lesser of (1) the excess (if any) of (a) the amount of cash received (excluding

any cash received in lieu of a fractional share of our common stock and any cash received attributable to accrued and unpaid interest) plus the fair market value of our common stock received (treating a fractional share of our common stock as issued and received for this purpose and excluding any common stock that is attributable to accrued and unpaid interest) upon conversion over (b) the U.S. Holder s adjusted tax basis in the converted note, and (2) the amount of cash received upon conversion (other than any cash received in lieu of a fractional share of our common stock and any cash received attributable to accrued and unpaid interest). Subject to the discussion under Constructive Distributions below regarding the possibility that certain adjustments to the conversion rate of a note may be treated as a taxable dividend, any gain recognized by a U.S. Holder upon conversion of a note will be long-term capital gain if the U.S. Holder held the note for more than one year, or short-term capital gain if the U.S. Holder held the note for one year or less, at the time of the conversion. Long-term capital gains of non-corporate taxpayers currently are taxed at reduced rates. Short-term capital gains are taxed at ordinary income rates. The U.S. Holder s tax basis in the common stock received (including any fractional share for which cash is paid, but excluding shares attributable to accrued and unpaid interest) generally would equal the adjusted tax basis of the converted note, decreased by the amount of cash received (other than cash in lieu of a fractional share of common stock and any cash attributable to accrued and unpaid interest), and increased by the amount of gain (if any) recognized upon conversion (other than any gain recognized as a result of cash received in lieu of a fractional share of common stock). The U.S. Holder s holding period in the common stock received (other than shares attributable to accrued and unpaid interest) would include the holding period in the converted note.

Alternatively, the conversion of a note into a combination of cash and shares of our common stock may be treated as in part a payment in redemption for cash of a portion of the note and in part a conversion of a portion of the note into common stock. In that case, a U.S. Holder s adjusted tax basis in the note would be allocated between the portion of the note treated as redeemed and the portion of the note treated as converted into common stock on a pro rata basis (based on relative fair market values). The U.S. Holder generally would recognize capital gain or loss with respect to the portion of the note treated as redeemed equal to the difference between the amount of cash received by the U.S. Holder (other than amounts attributable to accrued and unpaid interest) and the U.S. Holder s adjusted tax basis in the portion of the note treated as redeemed, subject to the discussion under Constructive Distributions below regarding the possibility that certain adjustments to the conversion rate of a note may be treated as a taxable dividend. See Sale, Exchange, Redemption or Other Taxable Disposition of Notes above. With respect to the portion of the note treated as converted, a U.S. Holder generally would not recognize any gain or loss (except with respect to cash received in lieu of a fractional share of common stock and common stock received attributable to accrued and unpaid interest), subject to the discussion under Constructive Distributions below regarding the possibility that certain adjustments to the conversion rate of a note may be treated as a taxable dividend. The tax basis allocated to the portion of the note treated as converted into common stock would be the U.S. Holder s tax basis in the common stock received (including any fractional share for which cash is paid, but excluding shares attributable to accrued and unpaid interest). The U.S. Holder s holding period in the common stock received (other than shares attributable to accrued and unpaid interest) would include the holding period in the converted note. All U.S. Holders should consult their own tax advisors regarding the tax consequences of the receipt of cash and common stock for notes upon conversion.

With respect to cash received in lieu of a fractional share of our common stock, a U.S. Holder would be treated as if the fractional share were issued and received and then immediately redeemed for cash. Accordingly, the U.S. Holder generally would recognize gain or loss equal to the difference between the cash received and that portion of the U.S. Holder s adjusted tax basis in the common stock attributable to the fractional share on a proportionate basis in accordance with its relative fair market value. Any such gain or loss generally would be capital gain or loss and would be long-term capital gain or loss, if at the time of the conversion, the notes had been held for more than one year.

Any cash and the fair market value of any portion of our common stock that is attributable to accrued and unpaid interest on the notes not yet included in income by a U.S. Holder would be taxed as ordinary income. The basis in any

shares of common stock attributable to accrued and unpaid interest not yet included in income would

equal the fair market value of such shares when received. The holding period in any shares of common stock attributable to accrued and unpaid interest would begin on the day after the date of conversion.

A U.S. Holder that converts a note between a record date for an interest payment and the next interest payment date and consequently receives a payment of cash interest, as described in Description of Notes Conversion Rights General, should consult its own tax advisor concerning the appropriate treatment of such payment.

If we undergo certain corporate transactions, as described under Description of Notes Conversion Rights Conversion Rate Adjustments above, the conversion obligation may be adjusted so that holders would be entitled to convert the notes into the type of consideration that they would have been entitled to receive upon such corporate transaction had the notes been converted into our common stock immediately prior to such corporate transaction, except that such holders will not be entitled to receive the additional shares resulting from the adjustment described under Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption unless such notes are converted in connection with the relevant make-whole fundamental change. Depending on the facts and circumstances at the time of such corporate transaction, such adjustment may result in a deemed exchange of the outstanding notes, which may be a taxable event for U.S. federal income tax purposes. Whether or not such an adjustment results in a deemed exchange, a conversion of a note into such consideration might be a taxable event. U.S. Holders are urged to consult their own tax advisors regarding the U.S. federal income tax consequences of such an adjustment upon a business combination or other corporate transaction.

Distributions

If, after a U.S. Holder acquires any of our common stock upon a conversion of a note, we make a distribution (other than certain pro rata distributions of our common stock) in respect of such common stock from our current or accumulated earnings and profits (as determined under U.S. federal income tax principles), the distribution will be treated as a dividend and will be includible in a U.S. Holder s income at the time such U.S. Holder is treated as receiving such distribution for U.S. federal income tax purposes. If the distribution exceeds our current and accumulated earnings and profits, the excess generally will be treated first as a tax-free return of the U.S. Holder s investment, up to the U.S. Holder s tax basis in its common stock, and, to the extent the amount of the distribution exceeds the U.S. Holder s tax basis, any remaining excess generally will be treated as capital gain from the sale or exchange of the common stock. If the U.S. Holder is a U.S. corporation, it would generally be able to claim a dividends-received deduction on a portion of any distribution taxed as a dividend, provided that certain holding period and other requirements are satisfied. Subject to certain exceptions, dividends received by non-corporate U.S. Holders generally are taxed at the reduced rates applicable to long-term capital gains, provided that certain holding period requirements are met.

Constructive Distributions

The terms of the notes allow for changes in the conversion rate of the notes under certain circumstances. A change in conversion rate that allows holders of notes to receive more shares of common stock on conversion may increase such U.S. Holders proportionate interests in our earnings and profits or assets. In that case, the U.S. Holders of notes may be treated as though they received a taxable distribution. A taxable constructive distribution could result, for example, if the conversion rate is adjusted to compensate U.S. Holders of notes for distributions of cash or property to our stockholders. The adjustment to the conversion rate of notes converted in connection with a make-whole fundamental change or notice of redemption, as described under Description of Notes Conversion Rights Increase in Conversion Rate upon Conversion upon a Make-Whole Fundamental Change or Notice of Optional Redemption above, also may be treated as a taxable stock distribution. If an event occurs that dilutes the interests of stockholders or increases the

interests of U.S. Holders of the notes and the conversion rate of the notes is not adjusted (or not adequately adjusted), the resulting increase in the proportionate interests of U.S. Holders of the notes also could be treated as a constructive distribution to holders

of the notes. Conversely, if an event occurs that dilutes the interests of the U.S. Holders of the notes and the conversion rate is not adjusted (or not adequately adjusted), the resulting increase in the proportionate interests of our stockholders could be treated as a taxable distribution to such stockholders.

Not all changes in the conversion rate that result in U.S. Holders of notes receiving more common stock on conversion, however, increase such U.S. Holders proportionate interests in our earnings and profits or assets. For instance, a change in conversion rate could simply prevent the dilution of the U.S. Holders interests upon a stock split or other change in capital structure. Changes of this type, if made pursuant to a bona fide reasonable adjustment formula, are not treated as constructive distributions. In addition, adjustments to the conversion rate of the notes that are not made in connection with other stockholders of the Company receiving a distribution of money or other property generally will not give rise to a constructive distribution. The amount of any taxable constructive distribution resulting from a change to, or failure to change, the conversion rate that is treated as a distribution would be treated for U.S. federal income tax purposes in the same manner as a distribution on our common stock paid in cash or other property, as described under Distributions above. It would result in a taxable dividend to the recipient to the extent of our current or accumulated earnings and profits (with the recipient s tax basis in its note or common stock (as the case may be) being increased by the amount of such dividend), with any excess treated as a tax-free return of the recipient s investment in its note or common stock (as the case may be) or as capital gain. U.S. Holders should consult their own tax advisors regarding whether any taxable constructive dividends would be eligible for the reduced rates (for non-corporate holders) or dividends-received deduction (for corporate holders) described in the previous paragraph, as the requisite applicable holding periods might not be considered to be satisfied.

We are currently required to report the amount of any deemed distributions on our website or to the IRS and to holders of notes not exempt from reporting. The IRS proposed regulations addressing the amount and timing of deemed distributions, as well as obligations of withholding agents and filing and notice obligations of issuers in respect of such deemed distributions. These regulations would generally provide that (i) the amount of a deemed distribution is the excess of the fair market value of the right to acquire stock over the fair market value immediately after the conversion rate adjustment of such right without the adjustment, (ii) the deemed distribution occurs at the earlier of the date the adjustment occurs under the terms of the note and the date of the actual distribution of cash or property that results in the deemed distribution, (iii) subject to certain limited exceptions, a withholding agent is required to impose any applicable withholding on deemed distributions and, if there is no associated cash payment, may set off its withholding obligations against payments on the notes (or, in some circumstances, any payments on our common stock) or sales proceeds received by or other funds or assets of an investor and (iv) we are required to report the amount of any deemed distributions on our website or to the IRS and to all holders of notes (including holders of notes that would otherwise be exempt from reporting). The final regulations will be effective for deemed distributions occurring on or after the date of adoption, but holders of notes and withholding agents may rely on them prior to that date under certain circumstances.

Possible Effect of a Consolidation or Merger

In certain situations, we may consolidate or merge into another entity (as described above under Description of Notes Consolidation, Merger or Sale of Assets). Depending on the circumstances, a change in the obligor of the notes (or a change in other terms of the notes as described in Conversion of Notes above) as a result of the consolidation or merger could result in a deemed exchange of the outstanding notes, which may be a taxable event for U.S. federal income tax purposes. U.S. Holders are urged to consult their own tax advisors regarding the U.S. federal income tax consequences of such a consolidation or merger.

Sale, Exchange or Other Taxable Disposition of Common Stock

A U.S. Holder generally will recognize capital gain or loss on a sale, exchange or other taxable disposition of common stock. The U.S. Holder s gain or loss will equal the difference between the proceeds received by it and its tax basis in the stock. The proceeds received by the U.S. Holder will include the amount of any cash and

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the fair market value of any other property received for the stock. The gain or loss recognized by a U.S. Holder on a sale, exchange or other taxable disposition of common stock will be long-term capital gain or loss if the U.S. Holder s holding period in the common stock is more than one year, or short-term capital gain or loss if the U.S. Holder s holding period in the common stock is one year or less, at the time of the transaction. Long-term capital gains of non-corporate taxpayers are currently taxed at reduced rates. Short-term capital gains are taxed at ordinary income rates. The deductibility of capital losses is subject to limitations.

Non-U.S. Holders

The following discussion is limited to the U.S. federal income tax consequences relevant to a non-U.S. Holder (as defined above).

Taxation of Interest

Payments of interest to non-U.S. Holders generally are subject to U.S. federal income tax at a rate of 30% (or a reduced or zero rate under the terms of an applicable income tax treaty between the United States and the non-U.S. Holder s country of residence), collected by means of withholding by the payor.

Provided a non-U.S. Holder does not fall within any of the specified categories below, payments of interest on the notes to most non-U.S. Holders, however, will qualify as portfolio interest, and thus, subject to the discussion below regarding backup withholding and FATCA (as defined below), will be exempt from U.S. federal income tax, including withholding of such tax, if the non-U.S. Holders certify their nonresident status as described below.

The portfolio interest exemption will not apply to payments of interest to a non-U.S. Holder that:

- owns, actually or constructively, applying certain attribution rules and pursuant to the conversion feature or otherwise, shares of our stock representing at least 10% of the total combined voting power of all classes of our stock entitled to vote;
- is a controlled foreign corporation (generally, a foreign corporation more than 50% of the stock of which (by vote or value) is owned, directly, indirectly, or constructively, by one or more U.S. persons that each owns, actually or constructively, at least 10% of the corporation s voting stock or at least 10% of the total value of shares of all classes of the corporation s stock) that is related, directly or indirectly, to us through sufficient actual or constructive stock ownership; or
- is engaged in the conduct of a trade or business in the United States to which such interest payments are effectively connected (see the discussion under Income or Gains Effectively Connected with a U.S. Trade or Business below).

The portfolio interest exemption, reduction of the withholding rate pursuant to the terms of applicable income tax treaty and several of the special rules for non-U.S. Holders described below apply only if the holder certifies its nonresident status. A non-U.S. Holder can generally meet this certification requirement by providing a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or other appropriate IRS Form W-8 to us or the applicable withholding agent prior to the payment. If the non-U.S. Holder holds the note through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to the agent.

Special certificate rules apply to non-U.S. Holders that are pass-through entities rather than corporations or individuals.

Sale, Exchange, Redemption, Conversion or Other Disposition of Notes or Common Stock

Subject to the discussions below regarding backup withholding and FATCA, non-U.S. Holders generally will not be subject to U.S. federal income or withholding tax on any gain realized on the sale, exchange, redemption, conversion or other disposition of notes or common stock (other than with respect to payments

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attributable to accrued and unpaid interest, which will be taxed as described under Taxation of Interest above), unless:

- the gain is effectively connected with the conduct by the non-U.S. Holder of a U.S. trade or business (and, generally, if an income tax treaty applies, is attributable to a U.S. permanent establishment maintained by the non-U.S. Holder), in which case the gain would be subject to tax as described below under Income or Gains Effectively Connected with a U.S. Trade or Business ;

- the non-U.S. Holder is an individual who is present in the United States for 183 days or more in the year of disposition and certain other conditions apply, in which case, except as otherwise provided by an applicable income tax treaty, the gain, which may be offset by certain U.S.-source capital losses, would be subject to a flat 30% tax (or lower applicable income tax treaty rate), even though the individual is not considered a resident of the United States; or

- the rules of the Foreign Investment in Real Property Tax Act (or FIRPTA), described below, treat the gain as effectively connected with a U.S. trade or business.

The FIRPTA rules may apply to a sale, exchange, redemption, conversion or other disposition of notes or common stock by a non-U.S. Holder if we are at any time within five years before the sale, exchange, redemption, conversion or other disposition (or, if shorter, the non-U.S. Holder s holding period for the notes or common stock disposed of), a United States real property holding corporation (or USRPHC). In general, we would be a USRPHC if interests in U.S. real property composed at least 50% of the fair market value of our assets. We believe that we currently are not, and will not become in the future, a USRPHC.

Dividends and Constructive Dividends

Dividends paid to a non-U.S. Holder on any common stock received on conversion of a note, and any taxable constructive dividends resulting from certain adjustments (or failures to make adjustments) to the number of shares of common stock to be issued on conversion (as described under U.S. Holders Constructive Distributions above) generally will be subject to U.S. withholding tax at a 30% rate. The withholding tax on dividends (including any taxable constructive dividends), however, may be reduced under the terms of an applicable income tax treaty between the United States and the non-U.S. Holder s country of residence. A non-U.S. Holder should demonstrate its eligibility for a reduced rate of withholding under an applicable income tax treaty by timely delivering a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or other applicable IRS Form W-8. A non-U.S. Holder that is eligible for a reduced rate of withholding under the terms of an applicable income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. In the case of constructive dividends, because there may be no cash from which to withhold the required amount, withholding may apply to interest payments or other payments or deliveries made with respect to the notes (or, in some circumstances, any payments on our common stock) or sales proceeds received by, or other funds or assets of, such holder. Dividends on the common stock that are effectively connected with a non-U.S. Holder s conduct of a U.S. trade or business are discussed below under Income or Gains Effectively Connected with a U.S. Trade or Business.

Income or Gains Effectively Connected with a U.S. Trade or Business

The preceding discussion of the U.S. federal income and withholding tax considerations of the ownership or disposition and conversion of the notes and the ownership and disposition of the common stock into which the notes

may be converted by a non-U.S. Holder assumes that the non-U.S. Holder is not treated as being engaged in a U.S. trade or business for U.S. federal income tax purposes. If any interest or constructive dividends on the notes, dividends on common stock or gain from the sale, exchange, redemption, conversion or other disposition of the notes or common stock is effectively connected with a U.S. trade or business conducted by the non-U.S. Holder, then the income or gain will be subject to U.S. federal income tax on a net income basis at the regular graduated rates and in the same manner applicable to U.S. Holders. If the non-U.S. Holder is eligible for the

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benefits of a tax treaty between the United States and the holder s country of residence, any effectively connected income or gain generally will be subject to U.S. federal income tax only if it is also attributable to a permanent establishment or fixed base maintained by the non-U.S. Holder in the United States. Payments of interest, dividends or constructive dividends that are effectively connected with a U.S. trade or business (and, if a tax treaty applies, attributable to a permanent establishment or fixed base), and therefore included in the gross income of a non-U.S. Holder, will not be subject to 30% withholding, provided that the non-U.S. Holder claims exemption from withholding by timely filing a properly executed IRS Form W-8ECI (or applicable successor form). If the non-U.S. Holder is a corporation (or an entity treated as a corporation for U.S. federal income tax purposes), that portion of its earnings and profits that is effectively connected with its U.S. trade or business generally also would be subject to a branch profits tax. The branch profits tax rate is generally 30%, although an applicable income tax treaty might provide for a lower rate.

FATCA

Sections 1471 through 1474 of the Code, together with the applicable Treasury Regulations issued thereunder and other applicable guidance (FATCA), impose a withholding tax on certain types of payments made to foreign financial institutions and certain other non-financial foreign entities as defined in the Code and applicable regulations. FATCA generally imposes a 30% withholding tax on interest income and constructive dividends on the notes, dividends on our common stock, or gross proceeds from the sale or other disposition of, the notes or common stock paid to a foreign financial institution or to non-financial foreign entity (whether as beneficial owner or intermediary), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations or (2) the non-financial foreign entity either certifies it does not have any substantial U.S. owners or furnishes identifying information regarding each substantial U.S. owner and such entity meets certain other specified requirements, or (3) an exemption applies.

Subject to the following sentence, if the payee is a foreign financial institution and an exemption does not apply, it must enter into an agreement with the U.S. Treasury requiring, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. If the applicable foreign country has entered into an intergovernmental agreement with the United States regarding FATCA, that agreement may permit the payee to report to that country rather than to the U.S. Treasury and obviate any need to enter into an agreement with the U.S. Treasury.

FATCA withholding generally applies to interest and constructive dividends on the notes and dividends on our common stock and may apply to gross proceeds from the disposition of notes or common stock. Regulations recently proposed by the IRS and the U.S. Treasury indicate an intention to eliminate the requirement of FATCA withholding on gross proceeds, and the U.S. Treasury has indicated that taxpayers may rely on those proposed regulations, notwithstanding the statutory requirement for such withholding set forth in the Code. Prospective investors should consult their own tax advisors regarding FATCA.

Backup Withholding and Information Reporting

The Code and the Treasury Regulations require those who make specified payments to report the payments to the IRS. Among the specified payments are interest, dividends (including constructive dividends) and proceeds paid by brokers to their customers. This reporting regime is reinforced by backup withholding rules, which require the payor to withhold from payments to certain recipients subject to information reporting if any such recipient has failed to provide a taxpayer identification number to the payor, furnished an incorrect identification number or repeatedly failed to report interest or dividends on tax returns. The backup withholding rate is currently 24%.

Payments of interest or dividends (including constructive dividends) to U.S. Holders of notes or common stock and payments made to U.S. Holders by a broker upon a sale of the notes or our common stock generally

will be subject to information reporting, and will be subject to backup withholding, unless the holder (1) is an exempt recipient, or (2) provides the payor with a correct taxpayer identification number, certifies that it is a U.S. person not subject to backup withholding and complies with applicable certification requirements. We must report annually to the IRS the interest and/or dividends (including constructive dividends) paid to each non-U.S. Holder and the tax withheld, if any, with respect to such interest and/or dividends, including any tax withheld pursuant to the rules described under Taxation of Interest and Dividends and Constructive Dividends above. Copies of these reports may be made available to tax authorities in the country where the non-U.S. Holder resides. Payments to non-U.S. Holders of dividends on our common stock or interest and constructive dividends on the notes may be subject to backup withholding unless the non-U.S. Holder certifies its non-U.S. status on a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or appropriate IRS Form W-8. Payments made to non-U.S. Holders by a broker upon a sale of the notes or our common stock will not be subject to information reporting or backup withholding as long as the non-U.S. Holder certifies its non-U.S. status or otherwise establishes an exemption.

Any amounts withheld from a payment to a U.S. Holder or non-U.S. Holder of notes or common stock under the backup withholding rules will be allowed as a refund or can be credited against any U.S. federal income tax liability of the holder, provided the required information is timely furnished to the IRS.

The preceding discussion of material United States federal income tax consequences is for general information only and is not tax advice. Accordingly, each investor should consult its own tax advisor as to particular tax consequences to it of purchasing, holding and disposing of the notes and the common stock, including the applicability and effect of any state, local or non-U.S. tax laws, and of any pending or subsequent changes in applicable laws.

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UNDERWRITING

Jefferies LLC (the underwriter) is acting as sole book-running manager of the offering. Subject to the terms and conditions stated in the underwriting agreement, the underwriter has agreed to purchase, and we have agreed to sell to the underwriter, the aggregate principal amount of notes set forth below.

Underwriter	Principal Amount of Notes
Jefferies LLC	$ 200,000,000.00
Total	$ 200,000,000.00

The underwriting agreement will provide that the obligations of the underwriter to purchase the notes included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriter is obligated to purchase all the notes (other than those covered by the option to purchase additional notes described below) if it purchases any of the notes. However, the underwriter is not required to take or pay for the notes covered by the underwriter s option to purchase additional notes described below. The underwriter may offer and sell the notes through certain of its affiliates.

Option to Purchase Additional Notes

We have granted to the underwriter an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to $30,000,000 aggregate principal amount of additional notes at the public offering price less the underwriting discount, solely to cover over-allotments, if any.

Underwriting Discounts and Expenses

The underwriter proposes to offer the notes directly to the public at the public offering price set forth on the cover page of this prospectus supplement and some of the notes to dealers at the public offering price less a concession not to exceed $21 per $1,000 principal amount of the notes. After the initial offering, the public offering price and concession or any other selling term of this offering may be changed. No such change shall change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table summarizes the compensation we will pay to the underwriter.

	Per Note	No Exercise	Full Exercise
Public offering price	$ 1,000.00	$ 200,000,000.00	$ 230,000,000.00
Underwriting discounts and commissions paid by us	$ 35.00	$ 7,000,000.00	$ 8,050,000.00
Proceeds, before expenses, to us	$ 965.00	$ 193,000,000.00	$ 221,950,000.00

We estimate that our total expenses for this offering, excluding the underwriting discounts, will be approximately $700,000.

We and the underwriter have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriter may be required to make because of any of these liabilities.

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Lock-Up Agreement

We and all directors and executive officers and certain holders of our outstanding common stock have agreed that, without the prior written consent of the underwriter, we and they will not, during the period ending 60 days after the date of this prospectus supplement (the Restricted Period):

- sell, offer to sell, contract to sell or lend, effect any short sale or establish or increase a put equivalent position or liquidate or decrease any call equivalent position, pledge, hypothecate or grant any security interest in, or in any other way transfer or dispose of, in each case whether effected directly or indirectly, any common stock, any rights to acquire common stock or any securities convertible into or exercisable or exchangeable for common stock.

- enter into any swap;

- make any demand for, or exercise any right with respect to, the registration under the Securities Act of the offer and sale of any common stock or any securities convertible into or exercisable or exchangeable for common stock, or cause to be filed a registration statement, prospectus or prospectus supplement (or an amendment or supplement thereto) with respect to any such registration; or

- publicly announce any intention to do any of the foregoing during the Restricted Period;

- file any registration statement with the SEC relating to the offering of any common stock or any securities convertible into or exercisable or exchangeable for common stock; or

- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock;

The restrictions described in the immediately preceding paragraph do not apply to:

- the sale of the notes to the underwriter;

- the entry into and transactions described in Description of Share Lending Agreement ;

- any shares of our common stock issued by us upon the exercise of an option or warrant or the conversion of a security outstanding on the date hereof;

- any shares issued or options to purchase shares granted pursuant to existing employee benefit plans;

any shares issued pursuant to any non-employee director stock plan or dividend reinvestment plan;

any shares or any securities convertible into or exercisable or exchangeable for shares issued in connection with acquisitions, joint ventures and similar types of arrangements of up to 5% of outstanding shares in aggregate on the date hereof, as long as the recipients of such securities also agree not to sell or transfer those securities without the prior written consent of the underwriter for a period of 60 days from the date hereof;

the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act, provided that (x) no public announcement or filing is voluntarily made or required regarding such plan during the Restricted Period and (y) no shares or related securities are sold pursuant to such plan during the Restricted Period;

644,330 shares of our common stock that may be issuable to the sellers of Claros Diagnostics Inc. in connection with the approval of the Sangia Total PSA Test using the Claros Analyzer; or

certain other related transfers of shares of our common stock or related securities with respect to our directors and officers.

Jefferies LLC, in its discretion, may release the common stock, notes and other securities subject to the lock-up agreements described above in whole or in part at any time.

Listing

The notes will not be listed on any securities exchange or quoted on any automated dealer quotation system. The underwriter may make a market in the notes after completion of the offering, but will not be obligated to do so and may discontinue any market-making activities at any time without notice. No assurance can be given as to

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the liquidity of the trading market for the notes or that an active trading market for the notes will develop. If an active trading market for the notes does not develop, the market price and liquidity of the notes may be adversely affected.

Passive Market Making

In connection with this offering, the underwriter may engage in passive market making transactions in our common stock on the Nasdaq Global Select Market in accordance with Rule 103 of Regulation M under the Exchange Act during the period before the commencement of offers or sales of common stock and extending through the completion of distribution. A passive market maker must display its bids at a price not in excess of the highest independent bid of the security. However, if all independent bids are lowered below the passive market maker s bid that bid must be lowered when specified purchase limits are exceeded.

Price Stabilization, Short Positions and Penalty Bids

In connection with this offering, the underwriter may purchase and sell notes and common stock in the open market, including as a selling stockholder pursuant to related share lending arrangements. These transactions may include short sales, syndicate covering transactions and stabilizing transactions. Short sales involve syndicate sales of notes in excess of the aggregate principal amount of notes to be purchased by the underwriter in this offering, which creates a syndicate short position. Covered short sales are sales of notes made in an amount up to the aggregate principal amount of notes represented by the underwriter s option to purchase additional notes. In determining the source of notes to close out the covered syndicate short position, the underwriter will consider, among other things, the price of notes available for purchase in the open market as compared to the price at which it may purchase notes through the option to purchase additional notes. Transactions to close out the covered syndicate short position involve either purchases of notes in the open market after the distribution has been completed or the exercise of the option to purchase additional notes. The underwriter may also make naked short sales of notes in excess of the option to purchase additional notes. The underwriter must close out any naked short position by purchasing notes in the open market. A naked short position is more likely to be created if the underwriter is concerned that there may be downward pressure on the price of the notes in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of bids for or purchases of notes or common stock in the open market while this offering is in progress.

The underwriter also may impose a penalty bid. Penalty bids permit the underwriter to reclaim a selling concession from a syndicate member when the underwriter repurchases notes originally sold by that syndicate member in order to cover syndicate short positions or make stabilizing purchases.

Any of these activities may have the effect of preventing or retarding a decline in the market price of the notes and our common stock. They may also cause the price of the notes and our common stock to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriter may conduct these transactions on the Nasdaq Global Select Market or in the over-the-counter market or otherwise. If the underwriter commences any of these transactions, it may discontinue them at any time.

Other Relationships

The underwriter and its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriter and its respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses. In addition,

the underwriter (or its affiliates) will be entering into the transactions described under Description of Share Lending Agreement.

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In addition, in the ordinary course of their various business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for its own account and for the accounts of its customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriter and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Electronic Delivery

A prospectus supplement in electronic format may be made available on the website maintained by the underwriter, or selling group members, if any, participating in this offering. The underwriter may agree to allocate a limited principal amount of the notes for sale to its online brokerage account holders.

Selling Restrictions

European Economic Area

The notes are not intended to be offered, sold or otherwise made available to and should not be offered, sold or otherwise made available to any retail investor in the European Economic Area. For these purposes, a retail investor means a person who is one (or more) of: (i) a retail client as defined in point (11) of Article 4(1) of Directive 2014/65/EU (as amended, MiFID II); or (ii) a customer within the meaning of Directive 2002/92/EC, where that customer would not qualify as a professional client as defined in point (10) of Article 4(1) of MiFID II; or (iii) not a qualified investor as defined in Directive 2003/71/EC. Consequently, no key information document required by Regulation (EU) No 1286/2014 (as amended, the PRIIPs Regulation) for offering or selling the notes or otherwise making them available to retail investors in the European Economic Area has been prepared and therefore offering or selling the notes or otherwise making them available to any retail investor in the European Economic Area may be unlawful under the PRIIPs Regulation.

In relation to each member state of the European Economic Area (each, a Member State), no offer of any securities which are the subject of the offering contemplated by this prospectus supplement has been or will be made to the public in that Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the relevant competent authority in that Member State in accordance with the Prospectus Directive, except that an offer of such securities may be made to the public in that Member State:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the underwriter; or

(c) to any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the Company or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

This prospectus has been prepared on the basis that any offer of notes in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of notes. This prospectus is not a prospectus for the purposes of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any securities in any Member State means the communication in any form and by any means of sufficient information on the terms of

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the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive), and includes any relevant implementing measure in the Member State and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (FSMA) received by it in connection with the issue or sale of the notes in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the notes in, from or otherwise involving the United Kingdom.

This prospectus is for distribution only to persons who (i) have professional experience in matters relating to investments and who fall within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the Financial Promotion Order), (ii) are persons falling within Article 49(2)(a) to (d) of the Financial Promotion Order, or (iii) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of section 21 of the FSMA) in connection with the issue or sale of any notes may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as relevant persons). This prospectus is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this prospectus relates is available only to relevant persons and will be engaged in only with relevant persons.

Canada

The notes may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the notes must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws. Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser s province or territory for particulars of these rights or consult with a legal advisor. Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriter is not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Switzerland

The notes may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX) or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing

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Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the notes or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, us or the notes have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of notes will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and any offers of notes have not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of notes.

Korea

The notes have not been and will not be registered with the Financial Services Commission of Korea under the Financial Investment Services and Capital Markets Act of Korea. Accordingly, the notes have not been and will not be offered, sold or delivered, directly or indirectly, in Korea or to, or for the account or benefit of, any resident of Korea (as defined in the Foreign Exchange Transactions Law of Korea and its Enforcement Decree) or to others for re-offering or resale, except as otherwise permitted by applicable Korean laws and regulations. In addition, within one year following the issuance of the notes, the notes may not be transferred to any resident of Korea other than a qualified institutional buyer (as such term is defined in the Regulation on Issuance, Public Disclosure, etc. of securities of Korea, a Korean QIB) registered with the Korea Financial Investment Association (the KOFIA) as a Korean QIB and subject to the requirement of monthly reports with the KOFIA of its holding of Korean QIB bonds as defined in the Regulation on Issuance, Public Disclosure, etc. of notes of Korea, provided that (a) the notes are denominated, and the dividend payments thereunder are made, in a currency other than Korean won, (b) the amount of the securities acquired by such Korean QIBs in the primary market is limited to less than 20 per cent. of the aggregate issue amount of the notes, (c) the notes are listed on one of the major overseas securities markets designated by the Financial Supervisory Service of Korea, or certain procedures, such as registration or report with a foreign financial investment regulator, have been completed for offering of the securities in a major overseas securities market, (d) the one-year restriction on offering, delivering or selling of securities to a Korean resident other than a Korean QIB is expressly stated in the securities, the relevant underwriting agreement, subscription agreement and the offering circular and (e) the Company and the underwriter shall individually or collectively keep the evidence of fulfillment of conditions (a) through (d) above after having taken necessary actions therefor.

Brazil

For purposes of Brazilian law, this offer of securities is addressed to you personally, upon your request and for your sole benefit, and is not to be transmitted to anyone else, to be relied upon elsewhere or for any other purpose either quoted or referred to in any other public or private document or to be filed with anyone, without our prior express and written consent.

This offering does not constitute or form part of any public offering of notes in Brazil and, accordingly, has not been and will not be registered under Brazilian Federal Law No. 6385 of December 7, 1976, as amended, Brazilian Securities Commission (Comissão de Valores Mobiliários) Rule (Instrução) No. 400 of December 29, 2003, as amended, or under any other Brazilian securities law or regulation. Furthermore, our notes and we have not been and will not be registered with the Brazilian Securities Commission (Comissão de Valores Mobiliários) under Rule (Instrução) No. 480 of December 7, 2009, as amended.

Therefore, the notes offered hereby have not been, will not be and may not be offered for sale or sold in Brazil except in circumstances that do not constitute a public offering or other unauthorized distribution under applicable Brazilian laws and regulations. Documents relating to the notes, as well as the information contained therein, may not be supplied to the public as a public offering in Brazil or be used in connection with any offer for subscription or sale of the notes to the public in Brazil.

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Hong Kong

The notes have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a prospectus as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the notes has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to notes which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Singapore

This prospectus supplement has not been, and will not be, registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the notes may not be circulated or distributed, nor may the notes be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), pursuant to Section 274 of the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to the conditions set forth in the SFA.

Where the notes are subscribed or purchased under Section 275 of the SFA by a relevant person which is: (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries rights and interest (howsoever described) in that trust shall not be transferable for six months after that corporation or that trust has acquired the notes pursuant to an offer made under Section 275 of the SFA except: (1) to an institutional investor or to a relevant person defined in Section 275(1) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA; (2) where no consideration is or will be given for the transfer; (3) where the transfer is by operation of law; (4) as specified in Section 276(7) of the SFA; or (5) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

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LEGAL MATTERS

The validity of the notes offered hereby will be passed upon for us by Greenberg Traurig, LLP. Certain legal matters relating to this offering will be passed upon for the underwriter by Skadden, Arps, Slate, Meagher & Flom LLP, New York, New York.

EXPERTS

The consolidated financial statements of OPKO Health, Inc. and subsidiaries as of December 31, 2017 and 2016, and for each of the three years in the period ended December 31, 2017, and the effectiveness of internal control over financial reporting as of December 31, 2017, included in the OPKO Health, Inc. Current Report on Form 8-K dated January 28, 2019, and incorporated by reference in this prospectus and registration statement, have been audited by Ernst & Young LLP, independent registered certified public accounting firm, as set forth in their reports thereon (which contain an explanatory paragraph describing the adoption of Accounting Standards Update No. 2014-09, Revenue from Contracts with Customers (Topic 606), as described in Note 1 to the consolidated financial statements), and are incorporated herein by reference. Such consolidated financial statements are incorporated by reference herein in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Through our website at *www.opko.com*, you may access, free of charge, our filings, as soon as reasonably practical after we electronically file them with or furnish them to the SEC. The information contained in, or available through, our website is not incorporated by reference in, and should not be considered a part of, this prospectus supplement or the accompanying prospectus. Our SEC filings are also available to the public at the SEC s website at *www.sec.gov*.

The accompanying prospectus is part of a registration statement on Form S-3 that we filed with the SEC to register the securities offered hereby under the Securities Act. The accompanying prospectus does not contain all of the information included in the registration statement, including certain exhibits and schedules. You may obtain the registration statement and exhibits to the registration statement from the SEC at the address listed above or from the SEC s website listed above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information that we incorporate by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus automatically updates and supersedes previously filed information as applicable.

We incorporate by reference into this prospectus supplement and the accompanying prospectus the following documents filed by us with the SEC, other than any portion of any such documents that is not deemed filed under the Exchange Act in accordance with the Exchange Act and applicable SEC rules:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on March 1, 2018;

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our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2018, June 30, 2018 and September 30, 2018, filed with the SEC on May 8, 2018, August 7, 2018 and November 9, 2018;

our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 30, 2018; and

our Current Reports on Form 8-K filed with the SEC on March 1, 2018, April 4, 2018, April 9, 2018, April 27, 2018, June 22, 2018, September 10, 2018, September 11, 2018, September 14, 2018, November 9, 2018, December 27, 2018, January 8, 2019 and January 28, 2019.

In addition, all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (not including any information furnished under Item 2.02, 7.01 or 9.01 of Form 8-K and any other information that is identified as furnished rather than filed, which information is not incorporated by reference herein) prior to the termination of this offering, will be deemed to be incorporated herein by reference and to be a part of this prospectus supplement and the accompanying prospectus from the date of filing of such documents. Any statement contained in a document incorporated herein by reference will be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained herein, or in a subsequently filed document incorporated herein by reference, modifies or supersedes the statement. Any statement modified or superseded will not be deemed, except as modified or superseded, to constitute a part of this prospectus supplement and the accompanying prospectus.

We will provide without charge to each person, including any beneficial owner, to whom a prospectus supplement is delivered, upon written or oral request of that person, a copy of any and all of the information that has been incorporated by reference in this prospectus supplement and the accompanying prospectus but not delivered with this prospectus supplement (excluding exhibits unless specifically incorporated by reference into those documents). Please direct requests to us at the following address:

Opko Health, Inc.

Attention: Secretary

4400 Biscayne Boulevard

Miami, Florida 33137

(305) 575-4100

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PROSPECTUS

Common Stock

Preferred Stock

Debt Securities

Depositary Shares

Warrants

Purchase Contracts

Units

We or any selling stockholder may offer and sell from time to time, in one or more series or issuances and on terms that we will determine at the time of the offering, any combination of the securities described in this prospectus.

This prospectus provides you with a general description of the securities we or any selling stockholder may offer and sell. We will provide specific terms of any offering in a supplement to this prospectus. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you invest in any of our securities.

We or any selling stockholder may offer and sell in the same offering or in separate offerings; to or through underwriters, dealers and agents; or directly to purchasers. The names of any underwriters, dealers, or agents involved in the sale of our securities and any applicable fees, commissions, or discounts will be described in the applicable prospectus supplement. Our net proceeds from the sale of securities will also be set forth in the applicable prospectus supplement. We will not receive any proceeds from the sale of securities by selling stockholders.

This prospectus may not be used to consummate a sale of our securities unless accompanied by the applicable prospectus supplement.

Our common stock is listed on the Nasdaq Global Select Market of The Nasdaq Stock Market LLC under the symbol OPK.

Investing in our securities involves a high degree of risk. See the Risk Factors section beginning on page 1 of this prospectus for a discussion of information that should be considered in connection with an investment in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation

to the contrary is a criminal offense.

The date of this prospectus is January 28, 2019.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, utilizing a shelf registration process. Under this shelf registration process, we and/or selling stockholders may sell, from time to time, any combination of the securities described in this prospectus in one or more offerings. This prospectus provides you with general information regarding the securities we and/or selling stockholders may offer. We will provide a prospectus supplement that contains specific information about any offering by us and/or selling stockholders.

The prospectus supplement also may add, update, or change information contained in the prospectus. You should read both this prospectus and the prospectus supplement related to any offering as well as additional information described under the headings Where You Can Find More Information and Incorporation of Certain Information by Reference.

Neither we nor any selling stockholder has authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus or any accompanying prospectus supplement or any free writing prospectus. We and/or selling stockholders are offering to sell, and seeking offers to buy, securities only in jurisdictions where offers and sales are permitted. The information contained in this prospectus and in any accompanying prospectus supplement is accurate only as of the dates of their covers, regardless of the time of delivery of this prospectus or any prospectus supplement or of any sale of our securities. Our business, financial condition, results of operations, and prospects may have changed since those dates. You should rely only on the information contained or incorporated by reference in this prospectus or any accompanying prospectus supplement. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement, you should rely on the information in the prospectus supplement, provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference into this prospectus or any prospectus supplement the statement in the document having the later date modifies or supersedes the earlier statement.

Unless the context otherwise requires, the terms OPKO, Company, we, us, , our , or ours refer to OPKO Healt Delaware corporation, including its wholly-owned subsidiaries.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before making an investment decision, you should carefully consider the discussion of risks and uncertainties under the heading Risk Factors contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, which is incorporated by reference in this prospectus, and under similar headings in our subsequently filed Quarterly Reports on Form 10-Q, any Current Reports on Form 8-K that are filed with the SEC and Annual Reports on Form 10-K, as well as the other risks and uncertainties described in any applicable prospectus supplement or free writing prospectus and in the other documents incorporated by reference in this prospectus. See the sections entitled Where You Can Find More Information and Incorporation of Certain Information by Reference in this prospectus. The risks and uncertainties we discuss in this prospectus, in any applicable prospectus supplement or free writing prospectus and in the other documents incorporated by reference in this prospectus are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently believe are immaterial also may materially and adversely affect our business, financial condition and results of operations. Please also refer to the section of this prospectus titled Cautionary Statement About Forward Looking Statements.

CAUTIONARY STATEMENT ABOUT FORWARD-LOOKING STATEMENTS

This prospectus, any applicable prospectus supplement and the documents and information incorporated by reference herein and therein may contain forward-looking statements within the meaning of Section 27A of the

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Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Forward-looking statements may include, but are not limited to, statements relating to our objectives, plans and strategies as well as statements, other than historical facts, that address activities, events, or developments that we intend, expect, project, believe or anticipate will or may occur in the future. These statements are often characterized by terminology such as may, will, should, expects, plans, anticipates, could, intends, target, project believes, estimates, predicts, potential, or continue or the negative of these terms or other similar expressions.

Forward-looking statements are based on assumptions and assessments made in light of our experience and perception of historical trends, current conditions, expected future developments and other factors believed to be appropriate. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties, many of which are outside of our control. You should not place undue reliance on these forward-looking statements, which reflect our view only as of the date of this prospectus, and we undertake no obligation to update these forward-looking statements in the future, except as required by applicable law.

A number of important factors could cause actual results to differ materially from those indicated by the forward-looking statements, including, without limitation, those factors described under the heading Risk Factors in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, which is incorporated by reference in this prospectus, and under similar headings in our subsequently filed Quarterly Reports on Form 10-Q, any Current Reports on Form 8-K that are filed with the SEC and Annual Reports on Form 10-K, as well as the other risks and uncertainties described in any applicable prospectus supplement or free writing prospectus and in the other documents incorporated by reference in this prospectus. Some of the key factors that could cause actual results to differ from our expectations include the following:

- we have a history of losses and may not generate sustained positive cash flow sufficient to fund our operations and research and development programs;
- our need for, and ability to obtain, additional financing when needed on favorable terms, or at all;
- adverse results in material litigation matters or governmental inquiries, including, without limitation, recent lawsuits against us and our Chairman of the Board and Chief Executive Officer by the SEC, as well as related class action and derivative lawsuits;
- the risks inherent in developing, obtaining regulatory approvals for and commercializing new, commercially viable and competitive products and treatments;
- our research and development activities may not result in commercially viable products;
- that earlier clinical results of effectiveness and safety may not be reproducible or indicative of future results;
- the success of our relationship with Pfizer;

that we may fail to obtain regulatory approval for hGH-CTP or successfully commercialize *Rayaldee* and hGH-CTP;

that we may not generate profits or cash flow from our laboratory operations or substantial revenue from *Rayaldee* and our pharmaceutical and diagnostic products;

that currently available over-the-counter and prescription products, as well as products under development by others, may prove to be as or more effective than our products for the indications being studied;

our ability to build a successful pharmaceutical sales and marketing infrastructure;

our ability and our distribution and marketing partners ability to comply with regulatory requirements regarding the sales, marketing and manufacturing of our products and product candidates and the operation of our laboratories;

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the performance of our third-party distribution partners, licensees and manufacturers over which we have limited control;

our success is dependent on the involvement and continued efforts of our Chairman and Chief Executive Officer;

integration challenges for Transition Therapeutics, Inc., BioReference Laboratories, EirGen and other acquired businesses;

availability of insurance coverage with respect to material litigation matters;

changes in regulation and policies in the United States (U.S.) and other countries, including increasing downward pressure on healthcare reimbursement;

our ability to manage our growth and our expanded operations;

increased competition, including price competition;

changing relationships with payors, including the various state and multi-state Blues programs, suppliers and strategic partners;

efforts by third-party payors to reduce utilization and reimbursement for clinical testing services;

our ability to maintain reimbursement coverage for our products and services, including the 4Kscore test;

failure to timely or accurately bill and collect for our services;

failure in our information technology systems, including cybersecurity attacks or other data security or privacy incidents;

failure to obtain and retain new clients and business partners, or a reduction in tests ordered or specimens submitted by existing clients;

failure to establish, and perform to, appropriate quality standards to assure that the highest level of quality is observed in the performance of our testing services;

failure to maintain the security of patient-related information;

our ability to obtain and maintain intellectual property protection for our products;

our ability to defend our intellectual property rights with respect to our products;

our ability to operate our business without infringing the intellectual property rights of others;

our ability to attract and retain key scientific and management personnel;

failure to obtain and maintain regulatory approval outside the U.S.;

legal, economic, political, regulatory, currency exchange, and other risks associated with international operations; and

our ability to finance and successfully complete construction of a research, development and manufacturing center in Waterford, Ireland.

OUR COMPANY

We are a diversified healthcare company that seeks to establish industry-leading positions in large and rapidly growing medical markets. Our diagnostics business includes BioReference Laboratories, the nation s third-largest clinical laboratory with a core genetic testing business and an almost 400-person sales and marketing team to drive growth and leverage new products, including the 4Kscore prostate cancer test and the Claros 1 in-

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office immunoassay platform (in development). Our pharmaceutical business features Rayaldee, a U.S. Food and Drug Administration (FDA)- approved treatment for secondary hyperparathyroidism in adults with stage 3 or 4 chronic kidney disease and vitamin D insufficiency (launched in November 2016), OPK88004, a selective androgen receptor modulator currently being studied for benign prostatic hyperplasia but for which we are exploring other potential indications, and OPK88003, a once or twice weekly oxyntomodulin for type 2 diabetes and obesity which is a clinically advanced drug candidate among the new class of GLP-1 glucagon receptor dual agonists (phase 2b). Our pharmaceutical business also features hGH-CTP, a once-weekly human growth hormone injection (in phase 3 and partnered with Pfizer Inc. (Pfizer)).

We operate established pharmaceutical platforms in Spain, Ireland, Chile and Mexico, which are generating revenue and from which we expect to generate positive cash flow and facilitate future market entry for our products currently in development. We have a development and commercial supply pharmaceutical company, as well as a global supply chain operation and holding company in Ireland, which we expect will play an important role in the development, manufacturing, distribution and approval of a wide variety of drugs with an emphasis on high potency products. We also own a specialty active pharmaceutical ingredients manufacturer in Israel, which we expect will facilitate the development of our pipeline of molecules and compounds for our proprietary molecular diagnostic and therapeutic products.

We are a Delaware corporation. We maintain our principal executive offices at 4400 Biscayne Blvd., Miami, FL 33137. Our telephone number is (305) 575-4100. We maintain a website at *www.opko.com*. The information contained on our websites or that can be accessed through our website does not constitute part of this prospectus or the accompanying prospectus supplement.

USE OF PROCEEDS

Except as may be otherwise set forth in any prospectus supplement accompanying this prospectus, we will use the net proceeds we receive from sales of securities offered hereby to fund research and development to further develop and commercialize our portfolio of proprietary pharmaceutical and diagnostic products and for working capital, capital expenditures, acquisitions and other general corporate purposes, which may include the repayment or repurchase of indebtedness or debt securities outstanding from time to time. Pending these uses, the net proceeds may also be temporarily invested in cash equivalents or short-term securities. When specific securities are offered, the prospectus supplement relating thereto will set forth our intended use of the net proceeds that we receive from the sale of such securities.

SELLING STOCKHOLDERS

Selling stockholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire from us, our securities. Such selling stockholders may be parties to registration rights agreements with us, or we otherwise may have agreed or will agree to register their securities for resale. The initial purchasers of our securities, as well as their transferees, pledges, donees or successors, all of whom we refer to as selling stockholders, may from time to time offer and sell our securities pursuant to this prospectus and any applicable prospectus supplement.

The applicable prospectus supplement will set forth the name of each of the selling stockholders and the number of securities beneficially owned by such selling stockholder that are covered by such prospectus supplement. The applicable prospectus supplement will also disclose whether any of the selling stockholders has held any position or office with, has been employed by or otherwise has had a material relationship with us during the three years prior to the date of the applicable prospectus supplement.

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DILUTION

We will set forth in a prospectus supplement the following information regarding any material dilution of the equity interests of investors purchasing securities in an offering under this prospectus:

- the net tangible book value per share of our equity securities before and after the offering;
- the amount of the increase in such net tangible book value per share attributable to the cash payments made by purchasers of the equity interests being offered; and
- the amount of the immediate dilution from the public offering price which will be absorbed by such purchasers.

DESCRIPTION OF CAPITAL STOCK

General

This section describes the general terms of our capital stock. A prospectus supplement may provide information that is different from this prospectus. If the information in the prospectus supplement with respect to our stock being offered differs from this prospectus, you should rely on the information in the prospectus supplement. A copy of our amended and restated certificate of incorporation, as amended, which we refer to as our Amended and Restated Certificate of Incorporation, and our amended and restated bylaws, which we refer to as our Amended and Restated Bylaws, have been incorporated by reference from our filings with the SEC as an exhibit to the registration statement of which this prospectus forms a part. Our stock and the rights of the holders of our stock are subject to the applicable provisions of the General Corporation Law of the State of Delaware, which we refer to as the DGCL, our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws, as well as some of the terms of our outstanding indebtedness.

The description below of our stock and provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws are summaries and are qualified by reference to the Amended and Restated Certificate of Incorporation and our Amended and Restated Bylaws, and by the applicable provisions of the DGCL.

Our authorized capital stock consists of 760,000,000 shares of capital stock, of which: (i) 750,000,000 shares are designated as common stock, par value $0.01 per share; and (ii) 10,000,000 shares are designated as preferred stock, par value $0.01 per share. As of December 31, 2018, there were 586,331,543 shares of common stock issued and outstanding and no shares of preferred stock issued and outstanding.

Common Stock

Voting Rights

The holders of shares of our common stock are entitled to one vote per share in connection with the election of directors and all other matters submitted to a vote of stockholders. The holders of shares of our common stock do not have cumulative voting rights.

Dividend Rights

Subject to any preferential dividend rights of holders of any then outstanding shares of our preferred stock and our Amended and Restated Certificate of Incorporation, the holders of shares of our common stock shall be entitled to receive, on a pro rata basis, such dividends and other distributions in cash, stock or property when, as and if declared thereon by our board of directors from time to time out of our assets or funds legally available therefor. No dividends have been paid to holders of shares of our common stock since our incorporation, and no dividends are anticipated to be declared or paid in the reasonably foreseeable future.

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Liquidation Rights

After payments to creditors and subject to any preferential liquidation, dissolution or winding up rights of holders of any then outstanding shares of our preferred stock, the holders of shares of our common stock are entitled to share ratably in all of our remaining assets and funds available for distribution to holders of shares of our common stock upon the liquidation, dissolution or winding-up of our affairs.

Other Matters

Holders of shares of our common stock do not have any preemptive, subscription, redemption or conversion rights. All of the shares of our common stock currently issued and outstanding are fully-paid and nonassessable.

Preferred Stock

Under our Amended and Restated Certificate of Incorporation, our board of directors has the authority, without further action by stockholders, to divide shares of our preferred stock into such number of series as our board of directors may determine and to determine and alter, from time to time, the designations, rights, preferences, privileges and restrictions granted to and imposed upon any wholly unissued series of our preferred stock, including dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and the liquidation preference of any wholly unissued series of our preferred stock, any or all of which may be greater than the rights of our common stock, and to establish the number of shares constituting any such series. The issuance of preferred stock with voting rights or conversion rights may adversely affect the voting power of our common stock, including the loss of voting control to others. The issuance of preferred stock may also have the effect of delaying, deferring or preventing a change in control of our company without stockholder approval.

Series A Convertible Preferred Stock

Of the authorized preferred stock, 4,000,000 shares are designated Series A Convertible Preferred Stock . We redeemed all previously issued and outstanding shares of our Series A Convertible Preferred Stock.

Voting Rights

The holders of record of our Series A Convertible Preferred Stock were and would be entitled to notice of, and to vote on or consent to, all actions on which holders of shares of our common stock are required or permitted to act upon. On all matters requiring or permitting a vote or consent of the holders of common stock, each share of Series A Convertible Preferred Stock was and would be equivalent to one share of common stock and all shares of Series A Convertible Preferred Stock were and would be voted together with the shares of common stock as a single class, except as otherwise provided by our Amended and Restated Certificate of Incorporation or our Amended and Restated Bylaws or by law. So long as shares of Series A Convertible Preferred Stock were and would be outstanding, without the approval of the holders of record of at least a majority of the then outstanding shares of Series A Convertible Preferred Stock, voting separately as a class, we were not and would not be permitted to (i) alter or change the rights, preferences, privileges or restrictions of shares of Series A Preferred so as to affect them adversely; or (ii) increase the authorized number of shares of Series A Convertible Preferred Stock.

Dividend Rights

Holders of record of our Series A Convertible Preferred Stock were and would be entitled to receive dividends in the amount of $0.25 per share, payable annually in arrears. At the option of our board of directors, dividends were and would be payable to the extent lawfully permitted either (i) wholly or partially in cash or (ii) in newly issued shares of Series A Convertible Preferred Stock valued as set forth in our Amended and Restated Certificate of Incorporation.

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Liquidation Rights

In the event of a liquidation, dissolution or winding-up, the holders of record of our Series A Convertible Preferred Stock were and would be entitled to receive ratably in full, out of our lawfully available assets, an amount in cash per outstanding share of Series A Convertible Preferred Stock equal to the sum of $2.50 and all dividends (whether or not declared) accrued and unpaid thereon as of the date of final distribution to such holders, without interest, before any payment shall be made or any assets distributed to the holders of common stock or any other class or series of our capital stock ranking junior as to liquidation rights to the Series A Convertible Preferred Stock; provided, however, that such rights would accrue to the holders of Series A Convertible Preferred Stock only in the event our payments with respect to the liquidation preferences of any holders of capital stock ranking senior as to liquidation rights to our Series A Convertible Preferred Stock (the Senior Liquidation Stock) are fully met. If, upon any liquidation, dissolution and winding-up, the amount available for such payment to the holders of Series A Convertible Preferred Stock would not be sufficient to pay in full the amounts payable on the Series A Convertible Preferred Stock, the holders of the Series A Convertible Preferred Stock and any other class or series of the our capital stock which may be created having parity as to liquidation rights with the Series A Convertible Preferred Stock would share in the distribution of the amount available in proportion to the respective preferential amounts to which each is entitled.

The liquidation preference of our Series A Convertible Preferred Stock is subject to proportional adjustment as set forth in our Amended and Restated Certificate of Incorporation.

Conversion Rights

Each share of Series A Convertible Preferred Stock was and would be convertible, at the option of the holder of record, into fully paid and nonassessable shares of our common stock. Shares of Series A Convertible Preferred Stock were and would be convertible into the number of shares of our common stock determined by dividing (i) the number of shares of Series A Convertible Preferred Stock (including additional shares) held by a holder by (ii) a divisor equal to $2.50, subject to certain adjustments set forth in our Amended and Restated Certificate of Incorporation.

Optional Redemption

Shares of Series A Convertible Preferred Stock were and would be redeemable, at our option, in whole or in part, at any time and from time to time, if the average closing bid price of our common stock was at least $3.75 per share for any 30 consecutive trading days ending within 15 days prior to the date on which we give notice of redemption of shares of Series A Convertible Preferred Stock. The redemption price was and would be $2.50 per share plus a sum equal to the accrued but unpaid dividends on the Series A Convertible Preferred Stock.

Series C Convertible Preferred Stock

Of the authorized preferred stock, 500,000 shares are designated Series C Convertible Preferred Stock . All previously issued and outstanding shares of Series C Convertible Preferred Stock automatically converted into shares of our common stock, on a one hundred for one basis.

Voting Rights

Except as otherwise expressly provided in our Amended and Restated Certificate of Incorporation or as otherwise required by law, (i) each holder of Series C Convertible Preferred Stock was and would be entitled to vote on all matters submitted to a vote of our stockholders and was and would be entitled to that number of votes equal to the largest number of whole shares of common stock into which such holder s shares of Series C Convertible Preferred

Stock could be converted, at the record date for the determination of stockholders entitled to vote on such matters or, if no such record date is established, at the date such vote is taken or any written consent of stockholders is solicited, and (ii) the holders of shares of preferred stock and common stock would vote together (or tender written consents in lieu of a vote) as a single class on all matters submitted to our stockholders.

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Dividend Rights

The holders of shares of Series C Convertible Preferred Stock were and would be entitled to receive, when, as and if declared by our board of directors, out of our assets legally available therefor, prior and in preference to any declaration or payment of any dividend on our common stock or any other class or series of our capital stock ranking junior to the Series C Convertible Preferred Stock with respect to the payment of dividends, and subject to the rights to dividends of any class or series of our preferred stock ranking senior or on parity with our Series C Convertible Preferred Stock with respect to dividends, cumulative cash dividends at the rate per share as set forth in our Amended and Restated Certificate of Incorporation. Whenever we would declare a dividend on our common stock, the holders of the Series C Convertible Preferred Stock were and would be also entitled to receive dividends in an amount equal per share (on an as-if-converted to common stock basis) to the amount paid or set aside for each share of our common stock.

Liquidation Rights

In the event of any liquidation, dissolution or winding up, or in the event of our insolvency, distributions to our stockholders would be made in the following manner:

(i) First, before any distribution or payment is made to any holders of common stock or any other class or series of capital stock, the holders of Series C Convertible Preferred Stock would be entitled to be paid first out of the assets of the Company available for distribution to holders of capital stock of all classes and series, whether such assets are capital, surplus or earnings (collectively, Available Assets), an amount per share equal to the Series C Preferential Amount (as defined in our Amended and Restated Certificate of Incorporation).

(ii) After payment of the Series C Preferential Amount to all holders of the Series C Convertible Preferred Stock and payment of any other preference amounts to the holders of any other class or series of preferred stock entitled to a liquidation preference, the entire remaining Available Assets, if any, would be distributed among the holders of common stock, Series C Convertible Preferred Stock and any other class or series of preferred stock entitled to participate with the common stock in a liquidating distribution, pro rata in proportion to the shares of common stock then held by them and the shares of common stock which they then have the right to acquire upon conversion of such shares of preferred stock held by them.

Conversion Rights

The Series C Convertible Preferred Stock was and would be subject to conversion into shares of common stock at the option of the holder and upon certain specified events, in each case as set forth in our Amended and Restated Certificate of Incorporation.

8% Series D Cumulative Convertible Preferred Stock

Of the authorized preferred stock, 2,000,000 shares are designated 8% Series D Cumulative Convertible Preferred Stock (Series D Preferred Stock). All previously issued and outstanding shares of our Series D Preferred Stock were converted into shares of our common stock.

Voting Rights

The holders of Series D Preferred Stock had and would have the right to receive notice of any meeting of holders of our common stock or Series D Preferred Stock and to vote (on an as converted into common stock basis) upon any

matter submitted to a vote of the holders of common stock or Series D Preferred Stock. Except as otherwise expressly set forth in our Amended and Restated Certificate of Incorporation, the holders of Series D Preferred Stock would vote on each matter submitted to them with the holders of common stock and all other classes and series of our capital stock entitled to vote on such matter, taken together as a single class.

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Dividend Rights

Holders of shares of the Series D Preferred Stock were and would be entitled to receive, when, as and if declared by our board of directors, out of funds legally available therefor, dividends on each share of Series D Preferred Stock at a rate per annum equal to 8.0% of the sum of (i) $24.80 as adjusted in accordance with our Amended and Restated Certificate of Incorporation for each stock combination, stock split, recapitalization, or similar corporate action that is the functional equivalent of any of the foregoing, plus (ii) any and all declared and unpaid and accrued dividends thereon. All dividends described in the foregoing sentence were and would be cumulative, whether or not earned or declared, and accrued on an annual basis from the issue date of the Series D Preferred Stock. Whenever we would declare and pay or make a dividend or any other distribution on or with respect to shares of any class of our common stock, holders of shares of the Series D Preferred Stock were and would also be entitled to receive in respect of each share of Series D Preferred Stock, a dividend or distribution in an amount equal to the amount of such dividend or distribution received by a holder of the number of shares of our common stock for which such share of Series D Preferred Stock is convertible on the date of the payment of such dividend or distribution to holders of our common stock.

Rank and Liquidation Rights

With respect to dividend distributions (other than required dividends to the holders of our Series A Convertible Preferred Stock) and distributions upon liquidation, winding up or our dissolution, the Series D Preferred Stock ranked and would rank senior to all classes of our common stock, our Series A Convertible Preferred Stock, our Series C Convertible Preferred Stock and to each other class of our capital stock that is not specifically designated as ranking senior to or *pari passu* with our Series D Preferred Stock.

Conversion Rights

The Series D Preferred Stock was and would be subject to conversion into shares of common stock at the option of the holder and upon certain specified events, in each case as set forth in the certificate of designation with respect to the Series D Preferred Stock.

Certain Amended and Restated Certificate of Incorporation and Bylaws Provisions

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our Amended and Restated Bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or one of its committees or other matters properly brought by a stockholder under Rule 14a-8 promulgated under the Exchange Act.

Special Meetings

Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws provide that, except as otherwise required by law, special meetings of the stockholders may only be called by the chairman of the board of directors, the Chief Executive Officer, or by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the whole board. Only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders.

No Cumulative Voting

Section 214 of the DGCL provides that the certificate of incorporation of any corporation may provide stockholders with the right to cumulate votes in the election of directors. Our Amended and Restated Certificate of Incorporation does not provide for cumulative voting of shares of our stock.

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Delaware Anti-Takeover Law

We are a Delaware corporation subject to Section 203 of the DGCL. Under Section 203, certain business combinations between a Delaware corporation whose stock is listed on a national securities exchange or held of record by more than 2,000 stockholders and an interested stockholder are prohibited for a three-year period following the date that such stockholder became an interested stockholder, unless:

- the corporation has elected in its certificate of incorporation not to be governed by Section 203;
- the business combination or the transaction which resulted in the stockholder becoming an interested stockholder was approved by the board of directors of the corporation before the date of the business combination or the date such stockholder became an interested stockholder, as applicable;
- upon consummation of the transaction that made such stockholder an interested stockholder, the interested stockholder owned at least 85% of the voting stock (as defined in Section 203) of the corporation outstanding at the commencement of the transaction excluding voting stock owned by directors who are also officers or held in employee benefit plans in which the employees do not have a confidential right to tender stock held by the plan in a tender or exchange offer; or
- the business combination is approved by the board of directors and by the stockholders (acting at a meeting and not by written consent) by the affirmative vote of at least 66-2/3% of the outstanding voting stock which is not owned (as defined in Section 203) by the interested stockholder.

The three-year prohibition also does not apply to some business combinations proposed by an interested stockholder following the announcement or notification of an extraordinary transaction involving the corporation and a person who had not been an interested stockholder during the previous three years or who became an interested stockholder with the approval of a majority of the corporation s directors. The term business combination is defined generally to include mergers or consolidations between a Delaware corporation and an interested stockholder, transactions with an interested stockholder involving the assets or stock of the corporation or its majority-owned subsidiaries and transactions which increase an interested stockholder s percentage ownership of stock, or other transaction resulting in a financial benefit to the interested stockholder. The term interested stockholder is defined generally as those stockholders who become beneficial owners of 15% or more of a Delaware corporation s voting stock, together with the affiliates or associates of that stockholder.

Listing

Our common stock is listed on the NASDAQ Global Select Market under the trading symbol OPK.

Transfer Agent and Registrar

The Transfer Agent and Registrar for our common stock is American Stock Transfer & Trust Company. The registrar and transfer agent for our preferred stock will be set forth in the applicable prospectus supplement.

DESCRIPTION OF DEBT SECURITIES

This prospectus describes certain general terms and provisions of the debt securities that we may offer under this prospectus and one or more prospectus supplements. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a prospectus supplement. The following description of debt securities will apply to the debt securities offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of debt securities may specify different or additional terms.

We may issue senior, senior subordinated, or subordinated debt securities. Senior securities will be direct obligation of ours and will rank equally and ratably in right of payment with other indebtedness of ours

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that is not subordinated. Senior subordinated securities will be subordinated in right of payment to the prior payment in full of senior indebtedness, as defined in the applicable prospectus supplement, and may rank equally and ratably with any other senior subordinated indebtedness. Subordinated securities will be subordinated in right of payment to senior subordinated securities.

We need not issue all debt securities of one series at the same time. Unless we provide otherwise, we may reopen a series, without the consent of the holders of such series, for issuances of additional securities of that series.

We will issue the senior debt securities and senior subordinated debt securities under a senior indenture, which we will enter into with a trustee to be named in the senior indenture, and we will issue the subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We use the term indenture or indentures to refer to both the senior indenture and the subordinated indenture. Each indenture will be subject to and governed by the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act, and we may supplement the indenture from time to time. Any trustee under any indenture may resign or be removed with respect to one or more series of debt securities, and we may appoint a successor trustee to act with respect to that series. We have filed a form of indenture as an exhibit to this registration statement, of which this prospectus forms a part. The terms of the senior indenture and subordinated indenture will be substantially similar, except that the subordinated indenture will include provisions pertaining to the subordination of the subordinated debt securities and senior subordinated debt securities to the senior debt securities and any other of our senior securities. The following statements relating to the debt securities and the indenture are summaries only, are subject to change, and are qualified in their entirety to the detailed provisions of the indenture, any supplemental indenture, and the discussion contained in any prospectus supplements.

General

The debt securities will be our direct obligations. We may issue debt securities from time to time and in one or more series as our board of directors may establish by resolution or as we may establish in one or more supplemental indentures. The particular terms of each series of debt securities will be described in a prospectus supplement relating to the series. We may issue debt securities with terms different from those of debt securities that we previously issued.

We may issue debt securities from time to time and in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will set forth in a prospectus supplement, relating to any series of debt securities being offered, the initial offering price, and the following terms of the debt securities:

- the title of the debt securities;
- the series designation and whether they are senior securities, senior subordinated securities, or subordinated securities;
- the aggregate principal amount of the debt securities and any limit on the aggregate amount of the series of debt securities;

the price or prices (expressed as a percentage of the aggregate principal amount) at which we will issue the debt securities and, if other than the principal amount of the debt securities, the portion of the principal amount of the debt securities payable upon the maturity of the debt securities;

the date or dates on which we will pay the principal on the debt securities;

the rate or rates (which may be fixed or variable) or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index, or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable, and any regular record date for the interest payable on any interest payment date;

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the place or places where principal, premium, if any, and any interest will be payable or the method of such payment and where the debt securities can be surrendered for transfer, exchange, or conversion;

the terms, if any, by which holders of the debt securities may convert or exchange the debt securities for our common stock, preferred stock, or any other security or property;

if convertible, the initial conversion price, the conversion period, and any other terms governing such conversion;

any subordination provisions or limitations relating to the debt securities;

any sinking fund requirements;

any obligation we have to redeem, purchase or repay the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the price or prices at which and the period and periods within which and the terms and conditions upon which debt securities of the series shall be redeemed, purchased, or repaid pursuant to such obligation;

the dates on which and the price or prices at which we will repurchase the debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;

the denominations in which the debt securities will be issued, if other than denominations of $1,000 and any integral multiple thereof;

the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

whether we will issue the debt securities in certificated or book-entry form;

the price or prices at which (if any), the period or periods within which (if any), and the terms and conditions upon which (if other than as provided herein) the debt securities may be redeemed, in whole or in part, at the option, or as an obligation, of the Company;

whether the debt securities shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual debt securities, and the depositary for such global security and securities;

whether the debt securities will be in registered or bearer form and, if in registered form, whether the securities will be issuable, in whole or in part, in the form of a global security;

the currency of denomination of the debt securities;

the designation of the currency, currencies, or currency units in which payment of principal of, premium, and interest on the debt securities will be made;

if payments of principal of, and interest and any additional amounts on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the manner in which the amounts of payment of principal of, premium or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index, or financial index;

any applicability of the defeasance provisions described in this prospectus or any prospectus supplement;

the trustee for the debt securities;

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whether and under what circumstances, if any, we will pay additional amounts on any debt securities in respect of any tax, assessment, or governmental charge and, if so, whether we will have the option to redeem the debt securities instead of making this payment;

any addition to or change in the events of default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;

any addition to or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;

if the debt securities are to be issued upon the exercise of debt warrants, the time, manner, and place for them to be authenticated and delivered;

any securities exchange on which we will list the debt securities;

any restrictions on transfer, sale, or other assignment;

any provisions relating to any security provided for the debt securities;

any provisions relating to any guarantee of the debt securities;

any other terms of the debt securities, which may modify or delete any provision of the indenture as it applies to that series; and

any depositaries, interest rate calculation agents, exchange rate calculation agents, or other agents with respect to the debt securities.

We may issue debt securities that are exchangeable for or convertible into shares of our common stock or other securities or property. The terms, if any, on which the debt securities may be exchanged for or converted into shares of our common stock or other securities or property will be set forth in the applicable prospectus supplement. Such terms may include provisions for conversion, either mandatory, at the option of the holder or at our option, in which case the number of shares of common stock or other securities or property to be received by the holders of debt securities would be calculated as of a time and in the manner stated in the prospectus supplement.

We may issue debt securities at less than the principal amount payable upon maturity. We refer to these securities as original issue discount securities. If material or applicable, we will describe in the applicable prospectus supplement special U.S. federal income tax, accounting, and other considerations applicable to original issue discount securities.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and interest and any additional amounts on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will describe the restrictions, elections, general tax considerations, specific terms, and provide other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Except as may be set forth in any prospectus supplement relating to the debt securities, no indenture will contain any other provisions that would limit our ability to incur indebtedness or that would afford holders of the debt securities protection in the event of a highly leveraged or similar transaction involving us or in the event of a change in control. You should review carefully the applicable prospectus supplement for information with respect to events of default and any covenants applicable to the debt securities being offered.

Payments and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

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We will pay principal of, and interest and any additional amounts on, the debt securities of a particular series at the office of the paying agents designated by us, except that, unless we otherwise indicate in the applicable prospectus supplement, we may make interest payments by check, which we will mail to the holder, or by wire transfer to certain holders. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series.

Form, Transfer, and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, as depositary, or a nominee of the depositary (as a book-entry debt security), or a certificate issued in definitive registered form (as a certificated debt security), as described in the applicable prospectus supplement. Except as described under Global Debt Securities and Book-Entry System below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities

A holder of our debt securities may transfer or exchange certificated debt securities at the trustee s office or paying agencies in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

A holder of our debt securities may transfer certificated debt securities and the right to receive the principal of, and interest and any additional amounts on, certificated debt securities only by surrendering the old certificate representing those certificated debt securities and either we or the trustee will reissue the old certificate to the new holder, or we or the trustee will issue a new certificate to the new holder.

Global Debt Securities and Book-Entry System

Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the depositary, and registered in the name of the depositary or a nominee of the depositary. Ownership of beneficial interests in book-entry debt securities will be limited to persons that have accounts with the depositary for the related global debt security, whom we refer to as participants, or persons that may hold interests through participants.

Except as described in this prospectus or any applicable prospectus supplement, beneficial owners of book-entry debt securities will not be entitled to have securities registered in their names, will not receive or be entitled to receive physical delivery of a certificate in definitive form representing securities, and will not be considered the owners or holders of those securities under the indenture. Accordingly, to exercise any rights of a holder under the indenture, each person beneficially owning book-entry debt securities must rely on the procedures of the depositary for the related global debt security and, if that person is not a participant, on the procedures of the participant through which that person owns its interest.

We understand, however, that under existing industry practice, the depositary will authorize the persons on whose behalf it holds a global debt security to exercise certain rights of holders of debt securities, and the indenture provides that we, the trustee, and our respective agents will treat as the holder of a debt security the persons specified in a written statement of the depositary with respect to that global debt security for purposes of obtaining any consents or directions required to be given by holders of the debt securities pursuant to the indenture.

We will make payments of principal of, and interest and any additional amounts on, book-entry debt securities to the depositary or its nominee, as the case may be, as the registered holder of the related global debt security. We,

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the trustee, and any other agent of ours or agent of the trustee will not have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in a global debt security or for maintaining, supervising, or reviewing any records relating to such beneficial ownership interests.

Any certificated debt securities issued in exchange for a global debt security will be registered in such name or names as the depositary shall instruct the trustee. We expect that such instructions will be based upon directions received by the depositary from participants with respect to ownership of book-entry debt securities relating to such global debt security.

For additional discussion of book entry and certificated securities, see the section entitled Legal Ownership of Securities included in this prospectus. We have obtained the foregoing information in this section and the Legal Ownership of Securities section concerning the depositary and the depositary s book-entry system from sources we believe to be reliable. We take no responsibility for the depositary s performance of its obligations under the rules and regulations governing its operations.

No Protection in the Event of a Change in Control

Unless we provide otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

Covenants

Unless we provide otherwise in the applicable prospectus supplement, the debt securities will not contain any restrictive covenants, including covenants restricting us or any of our subsidiaries from incurring, issuing, assuming, or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries property or capital stock or restricting us or any of our subsidiaries from entering into any sale and leaseback transactions.

Merger, Consolidation, and Sale of Assets

Unless we provide otherwise in the applicable prospectus supplement, we may not merge with or into or consolidate with, or convey, transfer, or lease all or substantially all of our properties and assets to, any person (a successor person), unless the following applies:

- either (a) the company is the surviving entity or (b) the successor person is a corporation, partnership, trust, or other entity organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture;

- immediately after giving effect to the transaction, no event of default, and no event that, after notice or lapse of time, or both, would become an event of default, will have occurred and be continuing under the indenture; and

- certain other conditions that may be set forth in the applicable prospectus supplement are met.

This covenant would not apply to any recapitalization transaction, a change in control of us, or a transaction in which we incur a large amount of additional debt unless the transactions or change in control included a merger, consolidation, or transfer or lease of substantially all of our assets. Except as may be described in the applicable prospectus supplement, there are no covenants or other provisions in the indenture providing for a put right or increased interest or that would otherwise afford holders of debt securities additional protection in the event of a recapitalization transaction, a change in control of us, or a transaction in which we incur a large amount of additional debt.

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Events of Default Under the Indenture

Unless we provide otherwise in the applicable prospectus supplement, an event of default will mean, with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable and continuance of that default for a period of 30 days (unless the entire amount of such payment is deposited by us with the trustee or with a paying agent before the expiration of the 30-day period);

- default in the payment of principal of, and any other amounts due on, any debt security of that series when due and payable either at maturity, redemption, or otherwise;

- default in the deposit of any sinking fund payment, when and as due in respect of any debt security of that series;

- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series) or in the debt security, which default continues uncured for a period of 60 days after we receive written notice from the trustee or we and the trustee receive written notice from the holders of not less than a majority in principal amount of the outstanding debt securities of that series as provided in the indenture;

- we, pursuant to or within the meaning of any applicable bankruptcy law, commence a voluntary case, consent to the entry of an order for relief against us in an involuntary case, consent to the appointment of a custodian for all or substantially all of our property, make a general assignment for the benefit of our creditors, or admit in writing our inability generally to pay our debts as they become due; or, similarly, a court enters an order or decree under any applicable bankruptcy law that provides for relief against us in an involuntary case, appoints a custodian for all or substantially all of our properties, or orders our liquidation (and the order remains in effect for 60 days); and

- any other event of default provided with respect to debt securities of that series that is included in any supplemental indenture or is described in the applicable prospectus supplement accompanying this prospectus.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency, or reorganization) necessarily will constitute an event of default with respect to any other series of debt securities. An event of default may also be an event of default under our bank credit agreements or other debt securities in existence from time to time and under certain guaranties by us of any subsidiary indebtedness. In addition, certain events of default or an acceleration under the indenture may also be an event of default under some of our other indebtedness outstanding from time to time.

Unless we provide otherwise in the applicable prospectus supplement, if an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing (other than certain events of our bankruptcy, insolvency, or reorganization), then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by written notice to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of and accrued and unpaid interest, if any, of all debt securities of that series. In the case of an event of default resulting from certain events of bankruptcy, insolvency, or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, of all outstanding debt securities will become and be immediately due and payable without any declaration or other act by the trustee or any holder of outstanding debt securities.

At any time after an acceleration with respect to debt securities of a series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of not less than a majority

in principal amount of the outstanding debt securities of that series may cancel the acceleration and annul its consequences if the rescission would not conflict with any judgment or decree and if all existing events of default with respect to that series have been cured or waived except nonpayment of principal (or such lesser amount) or interest that has become due solely because of the acceleration.

The indenture also provides that the holders of not less than a majority in principal amount of the outstanding debt securities of any series may waive any past default with respect to that series and its consequences, except a default involving the following:

- our failure to pay the principal of, and interest and any additional amounts on, any debt security; or
- a covenant or provision contained in the indenture that cannot be modified or amended without the consent of the holders of each outstanding debt security affected by the default.

The trustee is generally required to give notice to the holders of debt securities of each affected series within 90 days of a default actually known to a responsible officer of the trustee unless the default has been cured or waived. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any default or event of default (except in payment on any debt securities of that series) with respect to debt securities of that series if it in good faith determines that withholding notice is in the interest of the holders of those debt securities.

Unless we provide otherwise in the applicable prospectus supplement, the indenture will provide that the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request or discretion of any holder of any such outstanding debt securities unless the trustee receives indemnity satisfactory to it against any loss, liability, or expense. Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method, and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. The trustee may, however, refuse to follow any discretion that conflicts with the indenture or any law or which may be unduly prejudicial to the holders of the debt securities of the applicable series not joining in the discretion.

Unless we provide otherwise in the applicable prospectus supplement, no holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing event of default with respect to debt securities of that series; and
- the holders of at least 25% in principal amount of the outstanding debt securities of that series have made written request, and offered reasonable indemnity, to the trustee to institute such proceeding as trustee, and the trustee will not have received from the holders of a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days.

Notwithstanding the foregoing, except as provided in the subordination provisions, if any, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, and any interest or additional amounts on, that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment.

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a certificate as to compliance with the indenture, or, in the event of noncompliance, specify the noncompliance and the nature and status of the noncompliance.

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Modification of Indenture and Waiver

Except as specified below, modifications and amendments to the indenture require the approval of not less than a majority in principal amount of our outstanding debt securities.

Changes Requiring the Unanimous Approval

We and the trustee may not make any modification or amendment to the indenture without the consent of the holder of each affected debt security then outstanding if that amendment will have any of the following results:

- reduce the rate of or extend the time for payment of interest on any debt security;
- reduce the principal of or change the fixed maturity of any debt security or waive a redemption payment or alter the redemption provisions on any debt security;
- reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal, interest, or any additional amounts on any debt security, except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from that acceleration;
- make the principal of, or interest or any additional amounts on, any debt security payable in currency other than that stated in the debt security;
- change the place of payment on a debt security;
- change the currency or currencies of payment of the principal of, and any premium, make-whole payment, interest, or additional amounts on, any debt security;
- impair the right to initiate suit for the enforcement of any payment on or with respect to any debt security;
- reduce the percentage of holders of debt securities whose consent is needed to modify or amend an indenture;

reduce the percentage of the holders of outstanding debt securities of any series necessary to modify or amend the indenture, to waive compliance with provisions of the indenture or defaults and their consequences under the indenture, or to reduce the quorum or voting requirements contained in the indenture;

make any change that adversely affects the right to convert or exchange any debt security other than as permitted by the indenture or decrease the conversion or exchange rate or increase the conversion or exchange price of any such debt security;

waive a redemption payment with respect to any debt security; or

make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, and interest and any additional amount on, those debt securities, the right of holders to institute suit for the enforcement of any payment or the right of holders to waive past defaults.

Changes Not Requiring Approval of Debt Holders

We and the trustee may modify or amend an indenture, without the consent of any holder of debt securities, for any of the following purposes:

to evidence the succession of another person to us as obligor under the indenture;

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to add to our existing covenants additional covenants for the benefit of the holders of all or any series of debt securities, or to surrender any right or power conferred upon us in the indenture;

to add events of default for the benefit of the holders of all or any series of debt securities;

to add or change any provisions of the indenture to facilitate the issuance of, or to liberalize the terms of, debt securities in bearer form, or to permit or facilitate the issuance of debt securities in uncertificated form, provided that this action will not adversely affect the interests of the holders of the debt securities of any series in any material respect;

to add, change, or eliminate any provisions of the indenture, provided that any addition, change, or elimination (a) shall neither (i) apply to any debt security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (ii) modify the rights of the holder of any debt security with respect to such provision, or (b) shall become effective only when there are no outstanding debt securities;

to establish additional series of debt securities;

to secure previously unsecured debt securities;

to establish the form or terms of debt securities of any series, including the provisions and procedures, if applicable, for the conversion or exchange of the debt securities into our common stock, preferred stock, or other securities or property;

to evidence and provide for the acceptance or appointment of a successor trustee or facilitate the administration of the trusts under the indenture by more than one trustee;

to make any provision with respect to the conversion or exchange of rights of holders pursuant to the requirements of the indenture;

to cure any ambiguity, defect, or inconsistency in the indenture, provided that the action does not adversely affect the interests of holders of debt securities of any series issued under the indenture;

to close the indenture with respect to the authentication and delivery of additional series of debt securities or to qualify, or maintain qualification of, the indenture under the Trust Indenture Act; or

to supplement any of the provisions of the indenture to the extent necessary to permit or facilitate defeasance and discharge of any series of debt securities, provided that the action shall not adversely affect the interests of the holders of the debt securities of any series in any material respect.

A vote by holders of debt securities will not be required for clarifications and certain other changes that would not adversely affect holders of the debt securities.

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance

Unless the terms of the applicable series of debt securities provide otherwise, we may be discharged from any and all obligations in respect of the debt securities of any series (except for certain obligations to register the transfer or exchange of debt securities of the series; to replace stolen, lost, or mutilated debt securities of the series; and to maintain paying agencies and certain provisions relating to the treatment of funds held by paying agents). We will be so discharged upon the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, foreign government obligations (as described at the end of this section), that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient to pay and discharge each installment of principal, interest, and any additional amounts on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of such payments in accordance with the terms of the indenture and those debt securities.

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This discharge may occur only if, among other things, we have delivered to the trustee an officers certificate and an opinion of counsel stating that we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that holders of the debt securities of such series will not recognize income, gain, or loss for U.S. federal income tax purposes as a result of the deposit, defeasance, and discharge and will be subject to U.S. federal income tax on the same amount and in the same manner and at the same times as would have been the case if the deposit, defeasance, and discharge had not occurred.

Defeasance of Certain Covenants

Unless the terms of the applicable series of debt securities provide otherwise, upon compliance with certain conditions, we may omit to comply with the restrictive covenants contained in the indenture (except for certain obligations to maintain paying agencies and certain provisions relating to the treatment of funds held by paying agents), as well as any additional covenants contained in the applicable prospectus supplement.

The conditions include, among others, the following:

depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, foreign government obligations, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient, in the opinion of a nationally recognized firm of independent public accountants, to pay principal, interest, and any additional amounts on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain, or loss for U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. federal income tax in the same amount and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

Covenant Defeasance and Events of Default

If we exercise our option, as described above, not to comply with certain covenants of the indenture with respect to any series of debt securities, and the debt securities of that series are declared due and payable because of the occurrence of any event of default, the amount of money and/or U.S. government obligations or foreign government obligations on deposit with the trustee will be sufficient to pay amounts due on the debt securities of that series at the time of their stated maturity but may not be sufficient to pay amounts due on the debt securities of that series at the time of the acceleration resulting from the event of default. However, we will remain liable for those payments.

Foreign government obligations means, with respect to debt securities of any series that are denominated in a currency other than U.S. dollars:

direct obligations of the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged, which are not callable or redeemable at the option of the issuer thereof; or

obligations of a person controlled or supervised by or acting as an agency or instrumentality of that government, the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by that government, which are not callable or redeemable at the option of the issuer thereof.

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Guarantees

Our payment obligations under any series of debt securities may be guaranteed by us or one or more of our subsidiaries. The terms of any such guarantee will be set forth in the applicable prospectus supplement.

Subordination

We will set forth in the applicable prospectus supplement the terms and conditions, if any, upon which any series of senior subordinated securities or subordinated securities is subordinated to debt securities of another series or to other indebtedness of ours. The terms will include a description of the following:

- the indebtedness ranking senior to the debt securities being offered;
- any restrictions on payments to the holders of the debt securities being offered while a default with respect to the senior indebtedness is continuing;
- any restrictions on payments to the holders of the debt securities being offered following an event of default; and
- provisions requiring holders of the debt securities being offered to remit some payments to holders of senior indebtedness.

Conversion and Exchange Rights

The terms on which debt securities of any series may be convertible into or exchangeable for our common stock, preferred stock, or other securities or property of our company will be described in the applicable prospectus supplement. These terms will include the following:

- the conversion or exchange price, or the manner of calculating the price;
- the exchange or conversion period;
- whether the conversion or exchange is mandatory, or voluntary at the option of the holder, or at our option;
- any restrictions on conversion or exchange in the event of redemption of the debt securities and any restrictions on conversion or exchange; and

the means of calculating the number of shares of our common stock, preferred stock, or other securities or property of our company to be received by the holders of debt securities.

The conversion or exchange price of any debt securities of any series that are convertible into our common stock or preferred stock may be adjusted for any stock dividends, stock splits, reclassification, combinations, or similar transactions, as set forth in the applicable prospectus supplement.

Redemption of Debt Securities

The debt securities may be subject to optional or mandatory redemption on terms and conditions described in the applicable prospectus supplement. Subject to such terms, we may opt at any time to redeem the debt securities in whole or in part.

If less than all the debt securities of any series are to be redeemed or purchased in an offer to purchase at any time, the trustee will select the debt securities of that series to be redeemed or purchased as follows: (1) if the securities of such series are listed on any national securities exchange, in compliance with the requirements of the principal national securities exchange on which the debt securities of that series are listed, or, (2) if the debt securities of that series are not listed on a national securities exchange, on a pro rata basis, by lot, or by such other method as the trustee deems fair and appropriate.

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Except as otherwise provided as to any particular series of debt securities, at least 30 days but not more than 60 days before a redemption date, we or the trustee will mail a notice of redemption to each holder whose debt securities are to be redeemed. From and after notice has been given as provided in the applicable indenture, if funds for the redemption of any debt securities called for redemption shall have been made available on the redemption date, the debt securities will cease to bear interest on the date fixed for the redemption specified in the notice, and the only right of the holders of the debt securities will be to receive payment of the redemption price.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the state of New York, except to the extent that the Trust Indenture Act is applicable.

DESCRIPTION OF DEPOSITARY SHARES

We may issue receipts for depositary shares representing fractional shares of preferred stock. The fractional share of the applicable series of preferred stock represented by each depositary share will be set forth in the applicable prospectus supplement.

The shares of any series of preferred stock underlying any depositary shares that we may sell under this prospectus will be deposited under a deposit agreement between us and a depositary selected by us. Subject to the terms of the deposit agreement, each holder of a depositary share will be entitled, in proportion to the applicable fraction of a share of the preferred stock underlying the depositary share, to all of the rights, preferences, and privileges, and will be subject to the qualifications and restrictions, of the preferred stock underlying that depositary share.

The depositary shares will be evidenced by depositary receipts issued under the deposit agreement. Depositary receipts will be distributed to the holders of the depositary shares that are sold in the applicable offering. We will incorporate by reference into the registration statement of which this prospectus forms a part the form of any deposit agreement, including a form of depositary receipt, that describes the terms of any depositary shares we are offering before the issuance of the related depositary shares. The following summaries of material provisions of the deposit agreement, the depositary shares and the depositary receipts are subject to, and qualified in their entirety by reference to, all of the provisions of the deposit agreement applicable to a particular offering of depositary shares. We urge you to read the prospectus supplements relating to any depositary shares that are sold under this prospectus, as well as the complete deposit agreement and depositary receipt.

Form

Pending the preparation of definitive depositary receipts, the depositary may, upon our written order, issue temporary depositary receipts substantially identical to the definitive depositary receipts but not in definitive form. These temporary depositary receipts will entitle their holders to all of the rights of definitive depositary receipts. Temporary depositary receipts will then be exchangeable for definitive depositary receipts at our expense.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions received with respect to the underlying preferred stock to the record holders of depositary shares in proportion to the number of depositary shares owned by those holders.

If there is a distribution other than in cash, the depositary will distribute property received by it to the record holders of depositary shares in proportion to the number of depositary shares owned by those holders, unless the

depositary determines that it is not feasible to do so. If this occurs, the depositary may, with our approval, sell the property and distribute the net proceeds from the sale to those holders in proportion to the number of depositary shares owned by them.

The amount distributed to holders of depositary shares will be reduced by any amounts required to be withheld by us or the preferred stock depositary on account of taxes or other governmental charges.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of our voluntary or involuntary liquidation, dissolution, or winding up, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Withdrawal of Underlying Preferred Stock

Except as otherwise provided in a prospectus supplement, holders may surrender depositary receipts at the principal office of the depositary and, upon payment of any unpaid amount due to the depositary, be entitled to receive the number of whole shares of underlying preferred stock and all money and other property represented by the related depositary shares. We will not issue any partial shares of preferred stock. If the holder delivers depositary receipts evidencing a number of depositary shares that represent more than a whole number of shares of preferred stock, the depositary will issue a new depositary receipt evidencing the excess number of depositary shares to the holder.

Redemption of Depositary Shares

If the preferred stock underlying any depositary shares we may sell under this prospectus is subject to redemption, the depositary shares will be redeemed from the proceeds received by the depositary resulting from any such redemption, in whole or in part, of that underlying preferred stock. The redemption price per depositary share will be equal to the applicable fraction of the redemption price per share payable with respect to the underlying preferred stock. Whenever we redeem shares of underlying preferred stock that are held by the depositary, the depositary will redeem, as of the same redemption date, the number of depositary shares representing the shares of underlying preferred stock so redeemed. If fewer than all of the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or proportionately, as may be determined by the depositary.

After the date fixed for redemption, the depositary shares called for redemption will no longer be deemed to be outstanding, and all rights of the holders of the depositary shares will cease, except the right to receive the monies payable and any other property to which the holders were entitled upon the redemption upon surrender to the preferred stock depositary of the depositary receipts evidencing the depositary shares. Any funds deposited by us with the preferred stock depositary for any depositary shares that the holders fail to redeem will be returned to us after a period of two years from the date the funds are deposited.

Voting

Upon receipt of notice of any meeting at which holders of the preferred stock underlying any depositary shares that we may sell under this prospectus are entitled to vote, the depositary will mail the information contained in the notice to the record holders of the depositary shares. Each record holder of the depositary shares on the record date, which will be the same date as the record date for the underlying preferred stock, will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the amount of the underlying preferred stock represented by the holder s

depositary shares. The depositary will then try, as far as practicable, to vote the number of shares of preferred stock underlying those depositary shares in accordance with those instructions, and

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we will agree to take all reasonable actions which may be deemed necessary by the depositary to enable the depositary to do so. The depositary will not vote the underlying preferred stock to the extent it does not receive specific instructions with respect to the depositary shares representing such preferred stock.

Conversion of Preferred Stock

If the prospectus supplement relating to any depositary shares that we may sell under this prospectus states that the underlying preferred stock is convertible into our common stock or other securities, the following will apply. The depositary shares, as such, will not be convertible into any of our securities. Rather, any holder of the depositary shares may surrender the related depositary receipts to the depositary with written instructions that direct us to cause conversion of the preferred stock represented by the depositary shares into or for whole shares of our common stock or other securities, as applicable. Upon receipt of those instructions and any amounts payable by the holder in connection with the conversion, we will cause the conversion using the same procedures as those provided for conversion of the underlying preferred stock. If only some of a holder s depositary shares are converted, a new depositary receipt or receipts will be issued to the holder for any depositary shares not converted.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may at any time be amended by agreement between us and the depositary. However, any amendment which materially and adversely alters the rights of the holders of depositary shares will not be effective until 90 days after notice of that amendment has been given to the holders. Each holder of depositary shares at the time any amendment becomes effective shall be deemed to consent and agree to that amendment and to be bound by the deposit agreement as so amended. The deposit agreement may be terminated by us or by the depositary only if all outstanding depositary shares have been redeemed or converted into any other securities into which the underlying preferred stock is convertible or there has been a final distribution, including to holders of depositary receipts, of the underlying preferred stock in connection with our liquidation, dissolution, or winding up.

Charges of Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangement. We will also pay charges of the depositary in connection with the initial deposit of the preferred stock, the initial issuance of the depositary shares, any redemption of the preferred stock, and all withdrawals of preferred stock by owners of depositary shares. Holders of depositary receipts will pay transfer, income, and other taxes and governmental charges and other specified charges as provided in the deposit arrangement for their accounts. If these charges have not been paid, the depositary may refuse to transfer depositary shares, withhold dividends and distributions, and sell the depositary shares evidenced by the depositary receipt.

Limitation on Liability

Neither we nor the depositary will be liable if either of us is prevented or delayed by law or any circumstance beyond our control in performing our respective obligations under the deposit agreement. Our obligations and those of the depositary will be limited to performance of our respective duties under the deposit agreement without, in our case, negligence or bad faith or, in the case of the depositary, negligence or willful misconduct. We and the depositary may rely upon advice of counsel or accountants, or upon information provided by persons presenting the underlying preferred stock for deposit, holders of depositary receipts, or other persons believed by us in good faith to be competent and on documents believed to be genuine.

Corporate Trust Office of Preferred Stock Depositary

The preferred stock depositary s corporate trust office will be set forth in the applicable prospectus supplement relating to a series of depositary shares. The preferred stock depositary will act as transfer agent and registrar for

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depositary receipts, and, if shares of a series of preferred stock are redeemable, the preferred stock depositary will act as redemption agent for the corresponding depositary receipts.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering notice to us of its election to resign. We may remove the depositary at any time. Any resignation or removal will take effect upon the appointment of a successor depositary and its acceptance of the appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having a combined capital and surplus of at least $50,000,000.

Reports to Holders

We will deliver all required reports and communications to holders of the preferred stock to the preferred stock depositary, and it will forward those reports and communications to the holders of depositary shares. Upon request, the preferred stock depositary will provide for inspection to the holders of depositary shares the transfer books of the depositary and the list of holders of receipts; provided that any requesting holder certifies to the preferred stock depositary that such inspection is for a proper purpose reasonably related to such person s interest as an owner of depositary shares evidenced by the receipts.

DESCRIPTION OF WARRANTS

General

We may issue warrants to purchase common stock, which we refer to as common stock warrants, preferred stock, which we refer to as preferred stock warrants, debt securities, which we refer to as debt security warrants, or depositary shares, which we refer to as depositary share warrants. Any of these warrants may be issued independently or together with any other securities offered by this prospectus and may be attached to or separate from those securities.

While the terms we have summarized below will generally apply to any future warrants we may offer under this prospectus, we will describe the particular terms of any warrants that we may offer in more detail in the applicable prospectus supplement. The terms of any warrants we offer under a prospectus supplement may differ from the terms we describe below.

We may issue the warrants under a warrant agreement, which we will enter into with a warrant agent to be selected by us. Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

We will incorporate by reference into the registration statement of which this prospectus forms a part the form of warrant agreement, including a form of warrant certificate, that describes the terms of the series of warrants we are offering before the issuance of the related series of warrants. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of

the warrant agreement applicable to a particular series of warrants. We urge you to read the applicable prospectus supplements related to the warrants that we sell under this prospectus, as well as the complete warrant agreements that contain the terms of the warrants.

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We will set forth in the applicable prospectus supplement the terms of the warrants in respect of which this prospectus is being delivered, including, when applicable, the following:

- the title of the warrants;
- the aggregate number of the warrants;
- the price or prices at which the warrants will be issued;
- the designation, number, and terms of the securities purchasable upon exercise of the warrants;
- the designation and terms of the other securities, if any, with which the warrants are issued and the number of warrants issued with each such security;
- the date, if any, on and after which the warrants and the related underlying securities will be separately transferable;
- the price at which each underlying security purchasable upon exercise of the warrants may be purchased;
- the date on which the right to exercise the warrants will commence and the date on which such right will expire;
- the minimum amount of the warrants that may be exercised at any one time;
- any information with respect to book-entry procedures;
- the effect of any merger, consolidation, sale, or other disposition of our business on the warrant agreement and the warrants;
- any other terms of the warrants, including terms, procedures, and limitations relating to the transferability, exchange, and exercise of such warrants;
- the terms of any rights to redeem or call, or accelerate the expiration of, the warrants;

the date on which the right to exercise the warrants begins and the date on which that right expires;

the U.S. federal income tax consequences of holding or exercising the warrants; and

any other specific terms, preferences, rights, or limitations of, or restrictions on, the warrants.

Unless specified in an applicable prospectus supplement, common stock warrants, preferred stock warrants, debt security warrants, or depositary shares warrants will be in registered form only.

A holder of warrant certificates may exchange them for new certificates of different denominations, present them for registration of transfer, and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any common stock warrants, preferred stock warrants, debt security warrants, or depositary shares warrants are exercised, holders of the warrants will not have any rights of holders of the underlying common stock, preferred stock, debt securities, or depositary shares, including any rights to receive dividends or to exercise any voting rights, except to the extent set forth under the heading Warrant Adjustments below.

Exercise of Warrants

Each warrant will entitle the holder to purchase for cash shares of common stock, preferred stock, debt securities, or depositary shares at the applicable exercise price set forth in, or determined as described in, the applicable prospectus supplement. Warrants may be exercised at any time up to the close of business on the expiration date set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

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Warrants may be exercised by delivering to the corporation trust office of the warrant agent or any other officer indicated in the applicable prospectus supplement (a) the warrant certificate properly completed and duly executed and (b) payment of the amount due upon exercise. As soon as practicable following exercise, we will forward the shares of common stock, preferred stock, debt securities, or depositary shares. If less than all of the warrants represented by a warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or a part of the exercise price for the warrants.

Amendments and Supplements to the Warrant Agreements

We may amend or supplement a warrant agreement without the consent of the holders of the applicable warrants to cure ambiguities in the warrant agreement, to cure or correct a defective provision in the warrant agreement, or to provide for other matters under the warrant agreement that we and the warrant agent deem necessary or desirable, so long as, in each case, such amendments or supplements do not materially and adversely affect the interests of the holders of the warrants.

Warrant Adjustments

Unless the applicable prospectus supplement states otherwise, the exercise price of, and the number of securities covered by, a common stock warrant, preferred stock warrant, debt security warrant, or depositary share warrant will be adjusted proportionately if we subdivide or combine our common stock, preferred stock, debt securities, or depositary shares, as applicable. In addition, unless the prospectus supplement states otherwise, if we, without payment:

- issue capital stock or other securities convertible into or exchangeable for common stock or preferred stock, or any rights to subscribe for, purchase, or otherwise acquire any of the foregoing, as a dividend or distribution to holders of our common stock or preferred stock;

- pay any cash to holders of our common stock or preferred stock other than a cash dividend paid out of our current or retained earnings or other than in accordance with the terms of the preferred stock;

- issue any evidence of our indebtedness or rights to subscribe for or purchase our indebtedness to holders of our common stock or preferred stock; or

- issue common stock or preferred stock or additional stock or other securities or property to holders of our common stock or preferred stock by way of spinoff, split-up, reclassification, combination of shares, or similar corporate rearrangement,

then the holders of common stock warrants, preferred stock warrants, debt security warrants, and depositary share warrants, as applicable, will be entitled to receive upon exercise of the warrants, in addition to the securities otherwise receivable upon exercise of the warrants and without paying any additional consideration, the amount of stock and other securities and property such holders would have been entitled to receive had they held our common stock, preferred stock, debt securities, or depositary shares, as applicable, issuable under the warrants on the dates on which holders of those securities received or became entitled to receive such additional stock and other securities and

property.

Except as stated above, the exercise price and number of securities covered by a common stock warrant, preferred stock warrant, debt security warrant, and depositary share warrant, and the amounts of other securities or property to be received, if any, upon exercise of those warrants, will not be adjusted or provided for if we issue those securities or any securities convertible into or exchangeable for those securities, or securities carrying the right to purchase those securities or securities convertible into or exchangeable for those securities.

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Holders of common stock warrants, preferred stock warrants, debt security warrants, and depositary share warrants may have additional rights under the following circumstances:

certain reclassifications, capital reorganizations, or changes of our common stock, preferred stock, or depositary shares, as applicable;

certain share exchanges, mergers, or similar transactions involving us and which result in changes of our common stock, preferred stock, or depositary shares, as applicable; or

certain sales or dispositions to another entity of all or substantially all of our property and assets.

If one of the above transactions occurs and holders of our common stock, preferred stock, debt securities, or depositary shares are entitled to receive stock, securities, or other property with respect to or in exchange for their securities, the holders of our common stock warrants, preferred stock warrants, debt security warrants, and depositary share warrants then outstanding, as applicable, will be entitled to receive upon exercise of their warrants the kind and amount of shares of stock and other securities or property that they would have received upon the applicable transaction if they had exercised their warrants immediately before the transaction.

DESCRIPTION OF PURCHASE CONTRACTS

We may issue purchase contracts, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or varying number of debt securities, shares of common stock or preferred stock, depositary shares, warrants, or any combination of the above, at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or varying number of debt securities, shares of common stock or preferred stock, depositary shares, warrants, or any combination of the above. The price of the securities subject to the purchase contracts may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula described in the purchase contracts. We may issue purchase contracts separately or as a part of units each consisting of a purchase contract and one or more of the other securities described in this prospectus or securities of third parties, including U.S. Treasury securities, securing the holder s obligations under the purchase contract. If we issue a purchase contract as part of a unit, the applicable prospectus supplement will state whether the purchase contract will be separable from the other securities in the unit before the purchase contract settlement date. The purchase contracts may require us to make periodic payments to holders or vice versa and the payments may be unsecured or pre-funded on some basis. The purchase contracts may require holders to secure the holder s obligations in a manner specified in the applicable prospectus supplement, and in certain circumstances, we may deliver newly issued prepaid purchase contracts, often known as prepaid securities, upon release to a holder of any collateral securing such holder s obligations under the original purchase contract.

We will incorporate by reference into the registration statement of which this prospectus forms a part the form of purchase contract we are offering before the issuance of the purchase contract. The following summaries of material provisions of the purchase contract are subject to, and qualified in their entirety by reference to, all the provisions of the purchase contract. We urge you to read the applicable prospectus supplements related to the purchase contracts that we sell under this prospectus, as well as the complete purchase contract.

The applicable prospectus supplement will describe the terms of any purchase contracts in respect of which this prospectus is being delivered, including, to the extent applicable, the following:

whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;

whether the purchase contracts are to be prepaid or not;

whether the purchase contracts will be issued as part of a unit and, if so, the other securities comprising the unit;

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whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance, or level of the securities subject to purchase under the purchase contract;

any acceleration, cancellation, termination, or other provisions relating to the settlement of the purchase contracts; and

whether the purchase contracts will be issued in fully registered or global form.

Material U.S. federal income tax consideration applicable to the purchase contracts and the purchase units will also be discussed in the applicable prospectus supplement.

DESCRIPTION OF UNITS

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. Units may be offered independently or together with common stock, preferred stock, debt securities, depositary shares, and warrants offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will generally apply to any future units that we may offer under this prospectus, we will describe the particular terms of any series of units that we may offer in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference into the registration statement of which this prospectus forms a part the form of unit agreement, including a form of unit certificate, if any, that describes the terms of the series of units we are offering before the issuance of the related series of units. The following summaries of material provisions of the units and the unit agreements are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the units that we sell under this prospectus, as well as the complete unit agreements that contain the terms of the units.

General

We may issue units consisting of common stock, preferred stock, debt securities, depositary shares, and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time, or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including the following:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions of the governing unit agreement that differ from those described below; and

any provisions for the issuance, payment, settlement, transfer, or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under Description of Capital Stock, Description of Debt Securities, Description of Depositary Shares, and Description of Warrants, will apply to each unit and to any common stock, preferred stock, debt security, depositary share, or warrant included in each unit, respectively.

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Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit, without the consent of the related unit agent or the holder of any other unit, may enforce by appropriate legal action its rights as holder under any security included in the unit.

Title

We, the unit agent, and any of their agents may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purposes and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depositary or warrant agent maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

See also the section entitled Description of Debt Securities Form, Transfer, and Exchange above for additional discussion of book entry and certificated form of ownership as such forms of ownership impact the rights and obligations of purchasers of debt securities to be issued under this prospectus.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers. Upon the issuance of a global security, the depositary will credit, on its book-entry registration and transfer system, the participants accounts with the respective principal amounts of the book-entry securities represented by the global security beneficially owned by such participants. The accounts to be credited will be designated by any dealers, underwriters, or agents participating in the distribution of the book-entry securities. Ownership of book-entry securities will be shown on, and the transfer of the ownership interests will be effected only through, records maintained by the depositary for the related global security (with respect to interests of participants) and on the records of participants (with respect to interests of persons holding through participants). The laws of some states may require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to own, transfer, or pledge beneficial interests in book-entry securities.

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Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker, or other financial institution that participates in the depositary s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker, or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he, she, or it maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers, and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name, or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations For Indirect Holders

If you hold securities through a bank, broker, or other financial institution, either in book-entry form or in street name, you should check with your own institution to determine the following:

- how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

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how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depositary s rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms. Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee, or a successor depositary, unless special termination situations arise. We describe those situations below under Special Situations When a Global Security Will Be Terminated. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank, or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

We may at any time and in our sole discretion determine not to have any of the book-entry securities of any series represented by one or more global securities and, in that event, we will issue certificated securities in exchange for the global securities of that series.

Special Considerations For Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor s financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his, her, or its name, and cannot obtain non-global certificates for his, her, or its interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his, her, or its own bank or broker for payments on the securities and protection of his, her, or its legal rights relating to the securities, as we describe above;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

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an investor may not be able to pledge his, her, or its interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

the depositary s policies, which may change from time to time, will govern payments, transfers, exchanges, and other matters relating to an investor s interest in a global security;

we and any applicable trustee have no responsibility for any aspect of the depositary s actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;

the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

financial institutions that participate in the depositary s book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices, and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable, or no longer qualified under the Exchange Act to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular types and series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We and/or any selling stockholder may sell the securities described in this prospectus from time to time in one or more of the following ways:

- to or through underwriters or dealers;
- directly to one or more purchasers;

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through agents; or

through a combination of any of those methods of sale.

The prospectus supplement with respect to the offered securities will describe the terms of the offering, including the following:

the name or names of any underwriters or agents;

any public offering price;

the proceeds from such sale;

any underwriting discounts or agency fees and other items constituting underwriters or agents compensation;

any over-allotment options under which underwriters may purchase additional securities from us and/or any selling stockholder;

any discounts or concessions allowed or reallowed or paid to dealers; and

any securities exchanges on which the securities may be listed.

We and/or any selling stockholder may distribute the securities from time to time in one or more of the following ways:

at a fixed public offering price or prices, which may be changed;

at prices relating to prevailing market prices at the time of sale;

at varying prices determined at the time of sale; or

at negotiated prices.

Unless otherwise indicated in the applicable prospectus supplement, if we and/or any selling stockholder use underwriters for a sale of securities, the underwriters will acquire the securities for their own account. The underwriters may resell the securities in one or more transactions, including negotiated transactions, at a fixed public offering price, or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the

securities will be subject to the conditions set forth in the applicable underwriting agreement. Unless otherwise indicated in a prospectus supplement, the underwriters will be obligated to purchase all the securities of the series offered if they purchase any of the securities of that series. We and/or any selling stockholder may change from time to time any initial public offering price and any discounts or concessions the underwriters allow or reallow or pay to dealers. We and/or any selling stockholder may use underwriters with whom we or they have a material relationship. We will describe in the prospectus supplement naming the underwriter the nature of any such relationship. We and/or any selling stockholder may designate agents who agree to use their reasonable efforts to solicit purchases for the period of their appointment or to sell securities on a continuing basis. We and/or any selling stockholder may also sell securities directly to one or more purchasers without using underwriters or agents.

Underwriters, dealers, or agents may receive compensation in the form of discounts, concessions, or commissions from us and/or any selling stockholder or from purchasers of the securities as their agents in connection with the sale of the securities. These underwriters, dealers, or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions, or profits on resale received by underwriters, dealers, or agents may be treated as underwriting discounts and commissions. Each prospectus supplement will identify any underwriter, dealer, or agent and describe any compensation received by them from us and/or any selling stockholder. Any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

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Unless otherwise specified in the applicable prospectus supplement, each class or series of securities will be a new issue with no established trading market, other than our common stock, which is listed on the Nasdaq Global Select Market. We may elect to apply for listing of our common stock on another securities exchange or to list any other class or series of securities on any exchange, but we are not obligated to do so. It is possible that one or more underwriters may make a market in a class or series of securities, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for any of the securities.

In connection with any offering, the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions, and penalty bids in accordance with Regulation M under the Exchange Act.

Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.

Over-allotment involves sales by the underwriters of shares of our common stock in excess of the number of shares the underwriters are obligated to purchase, which creates a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short position, the number of shares of our common stock over-allotted by the underwriters is not greater than the number of shares that they may purchase in the over-allotment option. In a naked short position, the number of shares of our common stock involved is greater than the number of shares in the over-allotment option. The underwriters may close out any covered short position by either exercising their over-allotment option or purchasing shares of our common stock in the open market.

Syndicate covering transactions involve purchases of our common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares of our common stock available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option so that if there is a naked short position, the position can only be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares of our common stock in the open market after the pricing of any offering that could adversely affect investors who purchase in that offering.

Penalty bids permit the representatives of the underwriters to reclaim a selling concession from a syndicate member when the common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These stabilizing transactions, over-allotments, syndicate covering transactions, and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on the Nasdaq Global Select Market or otherwise and, if commenced, may be discontinued at any time.

We and/or any selling stockholder may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we and/or any selling stockholder may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us and/or any selling stockholder or borrowed from us and/or any selling stockholder or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement.

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In addition, we and/or any selling stockholder may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

Underwriters, dealers, and agents may be entitled under agreements entered into with us to indemnification against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments they may be required to make in respect of these liabilities thereof. Underwriters, dealers, and agents and their affiliates may be customers of, may engage in transactions with, or perform services for us in the ordinary course of business for which they receive compensation.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon by Greenberg Traurig, LLP.

EXPERTS

The consolidated financial statements of OPKO Health, Inc. and subsidiaries as of December 31, 2017 and 2016, and for each of the three years in the period ended December 31, 2017, and the effectiveness of internal control over financial reporting as of December 31, 2017, included in the OPKO Health, Inc. Current Report on Form 8-K dated January 28, 2019, have been audited by Ernst & Young LLP, independent registered certified public accounting firm, as set forth in their reports thereon (which contain an explanatory paragraph describing the adoption of Accounting Standards Update No. 2014-09, *Revenue from Contracts with Customers (Topic 606),* as described in Note 1 to the consolidated financial statements*)*, and are incorporated herein by reference. Such consolidated financial statements are incorporated by reference herein in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Through our website at *www.opko.com*, you may access, free of charge, our filings, as soon as reasonably practical after we electronically file them with or furnish them to the SEC. The information contained in our website is not incorporated by reference in, and should not be considered a part of, this prospectus or any accompanying prospectus supplement. Our SEC filings are also available to the public at the SEC s website at *www.sec.gov*.

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC to register the securities to be offered hereby. This prospectus does not contain all of the information included in the registration statement, including certain exhibits and schedules. You may obtain the registration statement and exhibits to the registration statement from the SEC at the address listed above or from the SEC s website listed above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information that we incorporate by reference is considered to be part of this prospectus. Information that we file with the SEC in the future and

incorporate by reference in this prospectus automatically updates and supersedes previously filed information as applicable.

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We incorporate by reference into this prospectus the following documents filed by us with the SEC, other than any portion of any such documents that is not deemed filed under the Exchange Act in accordance with the Exchange Act and applicable SEC rules:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on March 1, 2018;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2018, June 30, 2018 and September 30, 2018, filed with the SEC on May 8, 2018, August 7, 2018 and November 9, 2018;
- our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 30, 2018; and
- our Current Reports on Form 8-K filed with the SEC on March 1, 2018, April 4, 2018, April 9, 2018, April 27, 2018, June 22, 2018, September 10, 2018, September 11, 2018, September 14, 2018, November 9, 2018, December 27, 2018, January 8, 2019 and January 28, 2019.

In addition, all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (not including any information furnished under Item 2.02, 7.01 or 9.01 of Form 8-K and any other information that is identified as furnished rather than filed, which information is not incorporated by reference herein), including those filings made after the date of the initial filing of the registration statement of which this prospectus forms a part, prior to the termination of the offering, will be deemed to be incorporated herein by reference and to be a part of this prospectus from the date of filing of such documents. Any statement contained in a document incorporated herein by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein, or in a subsequently filed document incorporated herein by reference, modifies or supersedes the statement. Any statement modified or superseded will not be deemed, except as modified or superseded, to constitute a part of this prospectus.

We will provide without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request of that person, a copy of any and all of the information that has been incorporated by reference in this prospectus but not delivered with this prospectus (excluding exhibits unless specifically incorporated by reference into those documents). Please direct requests to us at the following address:

OPKO Health, Inc.

4400 Biscayne Blvd.

Miami, Florida 33137

Attention: Secretary

Telephone: (305) 575-4100

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$200,000,000

OPKO Health, Inc.

4.50% Convertible Senior Notes due 2025

PROSPECTUS SUPPLEMENT

Jefferies LLC